L Number	Hits	Search Text	DB	Time stamp
1	7	(pyrimidin or pyrimidinyl) same valeric	USPAT; US-PGPUB	2003/10/01 10:37

EAST update 9/916,977

09/ 916,977

Welcome to STN International! Enter x:x

LOGINID:ssspta1202txn

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS	4	Jul 15	Data from 1960-1976 added to RDISCLOSURE
NEWS	5	Jul 21	Identification of STN records implemented
NEWS	6	Jul 21	Polymer class term count added to REGISTRY
NEWS	7	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS	8	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS	9	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS	10	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS	11	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS	12	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS	13	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS	14	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS	15	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS	16	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Righ Truncation
NEWS	17	AUG 18	Simultaneous left and right truncation added to ANABSTR
NEWS	18	SEP 22	DIPPR file reloaded
NEWS	19	SEP 25	INPADOC: Legal Status data to be reloaded
NEWS	20	SEP 29	DISSABS now available on STN

NEWS EXPRESS	April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 09:19:07 ON 01 OCT 2003

```
=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 09:19:20 ON 01 OCT 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   29 SEP 2003  HIGHEST RN 595542-94-2
DICTIONARY FILE UPDATES:  29 SEP 2003  HIGHEST RN 595542-94-2

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09916977.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1 ful
FULL SEARCH INITIATED 09:19:46 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 431374 TO ITERATE

 92.7% PROCESSED  400000 ITERATIONS                          3960 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.11

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       431374 TO   431374
PROJECTED ANSWERS:            4074 TO     4466

L2         3960 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       149.35     149.56
```

09/ 916,977

FILE 'CAPLUS' ENTERED AT 09:21:39 ON 01 OCT 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 1 Oct 2003 VOL 139 ISS 14
FILE LAST UPDATED: 30 Sep 2003 (20030930/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l2
L3 1280 L2

=> s l3 and integrin?
24952 INTEGRIN?
L4 47 L3 AND INTEGRIN?

=> d l4 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 47 ANSWERS - CONTINUE? Y/(N):n

=> d l4 1- ibib abs fhitstr
YOU HAVE REQUESTED DATA FROM 47 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:696685 CAPLUS
TITLE: Malonate-Claisen rearrangement for preparation of **integrin** receptor antagonist intermediates
INVENTOR(S): Humphrey, Guy R.; Farr, Roger N.; Lee, Jaemoon
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072042	A2	20030904	WO 2003-US5476	20030221

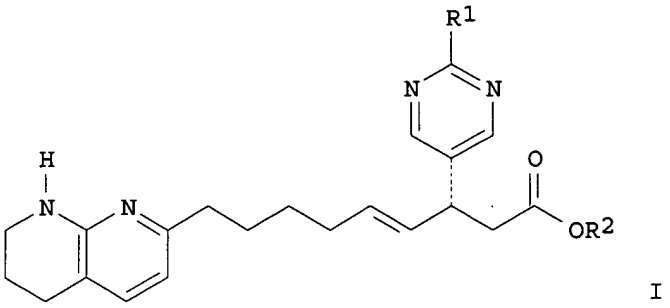
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

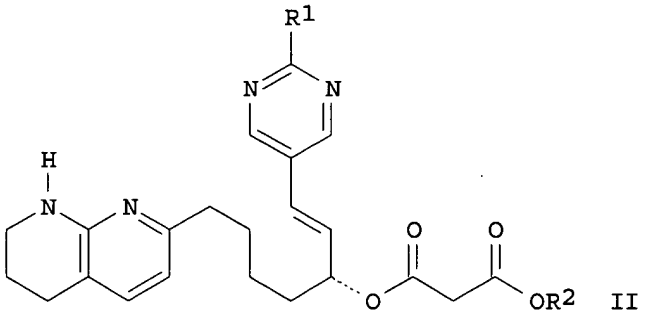
09/ 916,977

PRIORITY APPLN. INFO.: US 2002-360273P P 20020227

GI



I



II

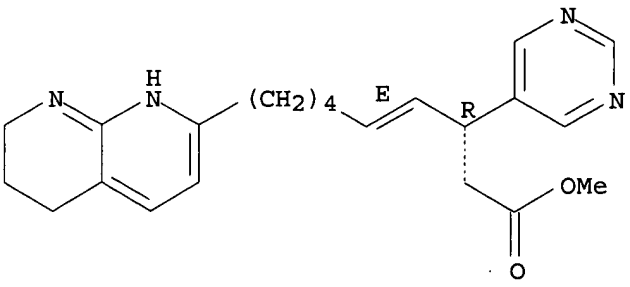
AB A process is described for the prepn. of chiral unsatd. ester intermediates [I; having the (R)-configuration at the stereogenic center marked with *;R1 = H, methyl; R2 = C1-4 alkyl, phenyl-C1-3-alkyl; e.g., 3-(R)-(pyrimidin-5-yl)-9-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)-(E)-non-4-enoic acid Me ester], useful in the asym. syntheses of .alpha.v.beta.3 **integrin** receptor antagonists (no data), which involves an efficient Claisen rearrangement of a malonate ester of a chiral allylic alc. precursor [II; e.g., Et malonate ester of (R)-1-(pyrimidin-5-yl)-7-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)-(E)-hept-1-en-3-ol] followed by hydrolysis and decarboxylation. The unsatd. ester intermediates can be converted in a 2-step sequence into the desired substituted nonanoic acid derivs. [e.g., 3-(S)-(pyrimidin-5-yl)-9-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)nonanoic acid Me ester].

IT **593282-80-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in a malonate-Claisen rearrangement for prepn. of **integrin** receptor antagonist intermediates)

RN 593282-80-5 CAPLUS

CN 5-Pyrimidinepropanoic acid, .beta.-[(1E)-6-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)-1-hexenyl]-, methyl ester, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L4 ANSWER 2 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:678514 CAPLUS
DOCUMENT NUMBER: 139:191440
TITLE: Methods of treating or preventing a cardiovascular condition using a cyclooxygenase-1 inhibitor
INVENTOR(S): Krul, Elaine S.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 32 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003162824	A1	20030828	US 2002-292255	20021112

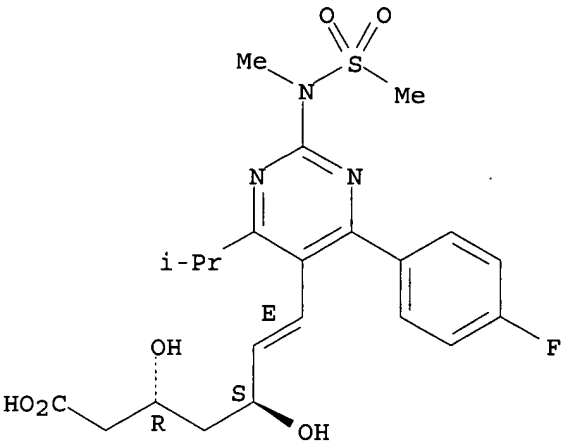
PRIORITY APPLN. INFO.: US 2001-331346P P 20011112
US 2001-338291P P 20011113

AB Methods for treating or preventing one or more cardiovascular conditions in a subject comprises treating the subject with a therapeutically effective amt. of a selective cyclooxygenase-1 inhibitor or a pharmaceutically-acceptable salt, tautomer or prodrug thereof alone or in combination with either a drug used in the treatment or prevention of a cardiovascular condition or a non-drug therapy used in the treatment of a cardiovascular condition. Cyclooxygenase-1 inhibitor, 5-(4-Chlorophenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)pyrazole (I), was prepd. from 4'-chloroacetophenone and (4-methoxyphenyl)hydrazine hydrochloride. I inhibited development of atherosclerosis in cholesterol-fed apoE knockout mice.

IT **287714-41-4**, Rosuvastatin
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid-lowering drug; cyclooxygenase-1 inhibitor for treating or preventing cardiovascular conditions)

RN 287714-41-4 CAPLUS
CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



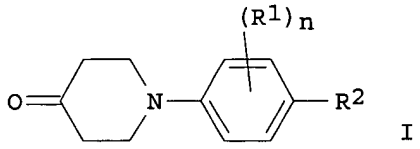
L4 ANSWER 3 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:570959 CAPLUS
DOCUMENT NUMBER: 139:133577
TITLE: Preparation of (4-oxopiperidin-1-yl)benzoic acid derivatives as intermediates for **integrin** -inhibiting phenylpiperidine derivatives
INVENTOR(S): Ishikawa, Minoru; Tsushima, Masaki; Yamada, Taku; Kubota, Dai; Yanagisawa, Yumiko; Hiraiwa, Yukiko; Ouchi, Shokichi; Anzai, Naomichi; Ajito, Keiichi
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003059883	A1	20030724	WO 2003-JP171	20030110

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-4089 A 20020111
OTHER SOURCE(S): MARPAT 139:133577
GI



I

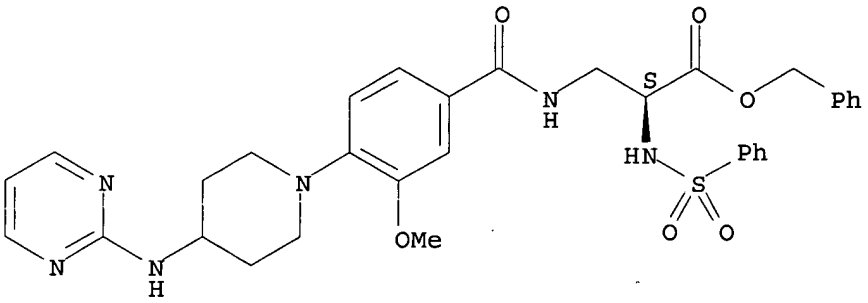
AB The title compds. I [R1 is C1-6 alkyl, C1-6 alkoxy, halogeno, amino, nitro, or hydroxyl;n is an integer; R2 is CO2R3, hydroxymethyl, or a nitrile group; and R3 is hydrogen, C1-6 alkyl, or aralkyl] are prepd. I are intermediates for **integrin** .alpha.v.beta.3-inhibiting phenylpiperidine derivs.

IT **568584-62-3P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of (4-oxopiperidin-1-yl)benzoic acid derivs. as intermediates for **integrin**-inhibiting phenylpiperidine derivs. and prepn. of said **integrin**-inhibiting phenylpiperidine derivs.)

RN 568584-62-3 CAPLUS

CN L-Alanine, 3-[[3-methoxy-4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:532140 CAPLUS
DOCUMENT NUMBER: 139:106450
TITLE: Targeted multivalent macromolecules
INVENTOR(S): Wartchow, Charles Aaron; Dechene, Neal Edward; Pease, John S.; Shen, Zhimin; Trulson, Julie; Bednarski, Mark David; Danthi, S. Narasimhan; Zhang, Michael; Choi, Hoyul Steven
PATENT ASSIGNEE(S): Targesome, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 71 pp., Cont.-in-part of U.S. Ser. No. 976,254.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003129223	A1	20030710	US 2002-158777	20020530

US 2002071843 A1 20020613 US 2001-976254 20011011
PRIORITY APPLN. INFO.: US 2000-239684P P 20001011
US 2001-294309P P 20010530
US 2001-309104P P 20010731
US 2001-312435P P 20010815
US 2001-976254 A2 20011011

AB Targeted therapeutic agents, comprising a linking carrier, a therapeutic entity assocd. with the linking carrier, and at least one targeting entity are provided, as well as methods for their prepn. and use. A targeted therapeutic agent is selected from matrix metalloprotease inhibitors, analgesics, aggrecanase inhibitors, alkylating agents, topoisomerase inhibitors, estrogens, androgens, interferons, intercalating agents, kinase modulators, etc. The linking carrier comprises a phosphatidylcholine and is selected from liposomes and a polymd. vesicle. A targeting entity targets a lipid construct to a target selected from a cell surface target, an intracellular target, and an extracellular matrix component. The targeting entity has, e.g., a vascular or tumor cell target selected from chemokine receptors, matrix metalloproteases, **integrins**, or prostate-specific membrane antigens. For example, **integrin**-targeted 90Y-labeled peptidomimetic vesicle complexes (IA-NP-Y90) at 5 .mu.Ci/g reduced tumor growth in a melanoma mouse model with av. normalized tumor vol. less than half the vol. in the buffer-treated animals. In addn., the av. tumor vol. quadrupling time (TVQT) for tumor treated with IA-NP-Y90 was 15.0 days compared to 6.4 days for tumors treated with buffer.

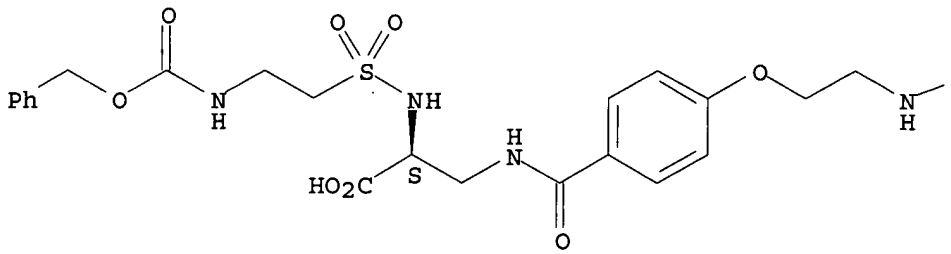
IT **477249-28-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of targeted multivalent macromols. for therapy, imaging and diagnosis of cancer)

RN 477249-28-8 CAPLUS

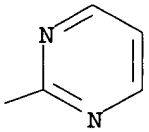
CN 2-Oxa-7-thia-4,8-diazadecan-10-oic acid, 3-oxo-1-phenyl-9-[[[4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]methyl]-, 7,7-dioxide, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L4 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:376627 CAPLUS
DOCUMENT NUMBER: 138:379262

09/ 916,977

TITLE: Compositions and methods for treating osteoporosis
INVENTOR(S): Stoch, Selwyn Aubrey; Orloff, John
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003039534	A1	20030515	WO 2002-US35341	20021104

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-337785P P 20011108

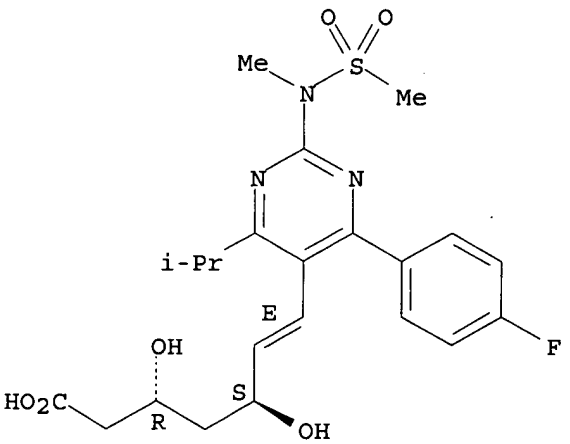
AB The present invention relates to pharmaceutical compns. comprising a cathepsin K inhibitor which are useful for treating such conditions as bone resorption, osteoporosis, arthritis, tumor metastases, Paget's disease, and other metabolic bone disorders characterized by increased bone resorption.

IT **287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for treating osteoporosis)

RN 287714-41-4 CAPLUS

CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



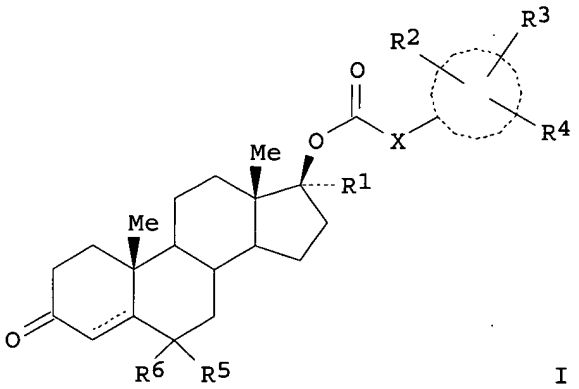
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:261603 CAPLUS
DOCUMENT NUMBER: 138:281598
TITLE: Androstane compounds as androgen receptor (AR) modulators for the treatment of AR-related diseases
INVENTOR(S): Wang, Jiabing
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003026568	A2	20030403	WO 2002-US29436	20020917

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-324124P P 20010921
OTHER SOURCE(S): MARPAT 138:281598
GI



I

AB Compds. of structural formula (I) as herein defined are claimed as useful in a method for modulating a function of the androgen receptor in a tissue selective manner in a patient in need of such modulation, as well as in a method of activating the function of the androgen receptor in a patient, and in particular the method wherein the function of the androgen receptor is blocked in the prostate of a male patient or in the uterus of a female patient and activated in bone and/or muscle tissue. These compds. are useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteopenia, osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male

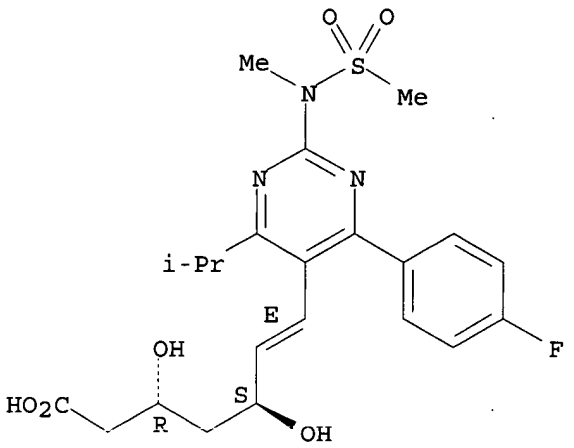
hypogonadism, female sexual dysfunction, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, aplastic anemia and other hematopoietic disorders, pancreatic cancer, renal cancer, prostate cancer, inflammatory arthritis and joint repair, alone or in combination with other active agents. Methods for the co-administration of those compds. with bone-strengthening agents are also claimed.

IT **287714-41-4**, Rosuvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(androstane compds. as androgen receptor (AR) modulators in conjunction with bone-strengthening agents for treatment of AR-related diseases)

RN 287714-41-4 CAPLUS

CN 6-Heptenoic acid, 7-[4-(4-fluorophenyl)-6-(1-methylethyl)-2-[methyl(methylsulfonyl)amino]-5-pyrimidinyl]-3,5-dihydroxy-, (3R,5S,6E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L4 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:977654 CAPLUS
DOCUMENT NUMBER: 138:61306
TITLE: Preparation of pharmaceuticals containing (pyrimidinyl)tetrahydronaphthyridinylnonanoic acid Tris salt as an **integrin** receptor antagonist
INVENTOR(S): Humphrey, Guy R.; Xu, Wei
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102374	A1	20021227	WO 2002-US18906	20020614

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003004171 A1 20030102 US 2002-174016 20020618

PRIORITY APPLN. INFO.: US 2001-299344P P 20010619

AB The tris(hydroxymethyl)aminomethane ("TRIS") salt of 3-(pyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-[1,8]-naphthyridin-2-yl)nonanoic acid is a potent antagonist of the **integrin** .alpha.v.beta.3 receptor and is useful for the prevention and/or treatment of osteoporosis and vascular restenosis, as well as conditions assocd. with excessive angiogenesis, such as macular degeneration, diabetic retinopathy, atherosclerosis, inflammatory arthritis, cancer, and metastatic tumor growth. The invention also relates to a process for the prepn. of the salt as well as pharmaceutical compns. contg. the salt and methods of using the salt. Thus, the 3R or 3S isomer of 3-(pyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-[1,8]-naphthyridin-2-yl)nonanoic acid was treated with tris(hydroxymethyl)aminomethane in EtOH soln. to give the title salts. The products were characterized by x-ray diffraction and FT-IR spectra and DSC. A 100-mg tablet is composed of 133 mg the active ingredient, 243 mg lactose, 20 mg croscarmellose sodium, and 4 mg magnesium stearate.

IT **479063-88-2P**

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of pharmaceuticals contg. (pyrimidinyl)tetrahydronaphthyridinyl nonanoic acid Tris salt as **integrin** receptor antagonist)

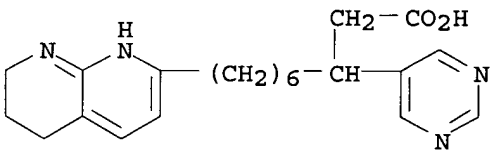
RN 479063-88-2 CAPLUS

CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, compd. with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 227753-43-7

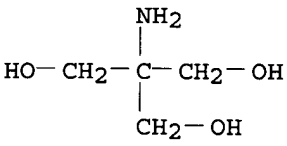
CMF C21 H28 N4 O2



CM 2

CRN 77-86-1

CMF C4 H11 N O3



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:943625 CAPLUS

DOCUMENT NUMBER: 138:368840

TITLE: Highly potent and selective .alpha.V.beta.3-receptor

antagonists: solid-phase synthesis and SAR of 1-substituted 4-amino-1H-pyrimidin-2-ones

AUTHOR(S): Zechel, Christian; Backfisch, Gisela; Delzer, Jurgen; Geneste, Herve; Graef, Claudia; Hornberger, Wilfried; Kling, Andreas; Lange, Udo E. W.; Lauterbach, Arnulf; Seitz, Werner; Subkowski, Thomas

CORPORATE SOURCE: BASF AG, Ludwigshafen, D-67056, Germany

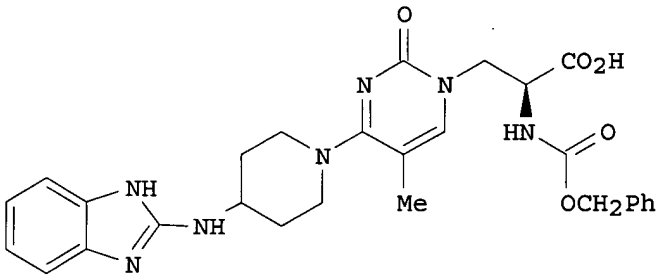
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(2), 165-169
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

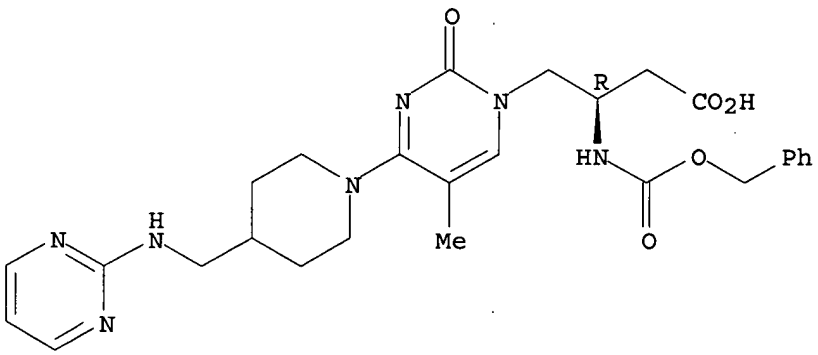
AB Solid-phase synthesis and SAR of .alpha.V.beta.3-receptor antagonists based on a N1-substituted 4-amino-1H-pyrimidin-2-one scaffold are described. The most potent compds., e.g. I, exhibited IC50 values towards .alpha.V.beta.3 in the nano- to subnanomolar range and high selectivity vs. related **integrins** like .alpha.IIb.beta.3. For selected examples efficacy in functional cellular assays was demonstrated.

IT **521273-57-4P**
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation)
(solid-phase synthesis and SAR of 1-substituted 4-amino-1H-pyrimidin-2-ones as .alpha.V.beta.3-receptor antagonists)

RN 521273-57-4 CAPLUS

CN 1(2H)-Pyrimidinebutanoic acid, 5-methyl-2-oxo-.beta.-[[(phenylmethoxy)carbonyl]amino]-4-[4-[(2-pyrimidinylamino)methyl]-1-piperidinyl]-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:927619 CAPLUS
DOCUMENT NUMBER: 138:8327
TITLE: .alpha.v.beta.3 **Integrin** receptor targeting liposome delivery system for nucleic acids
INVENTOR(S): Cheresh, David A.; Hood, John; Bednarski, Mark
PATENT ASSIGNEE(S): The Scripps Research Institute, USA; Board of Trustees of the Leland Stanford, Jr., University
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002097116	A2	20021205	WO 2002-US17157	20020530
WO 2002097116	A3	20030522		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003013674	A1	20030116	US 2002-159241	20020530
US 2003092655	A1	20030515	US 2002-158761	20020530

PRIORITY APPLN. INFO.: US 2001-294309P P 20010530
US 2001-345891P P 20011029

OTHER SOURCE(S): MARPAT 138:8327

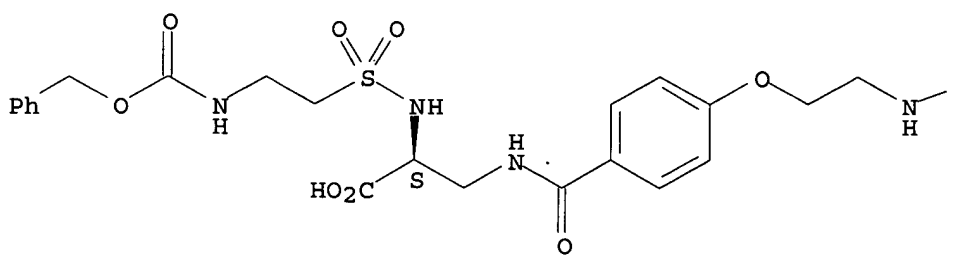
AB .alpha.v.beta.3 **Integrin** receptor targeting liposomes comprise a cationic amphiphile such as a cationic lipid, a neutral lipid, and a targeting lipid. The targeting lipid includes a non-peptidic .alpha.v.beta.3 **integrin** antagonist.

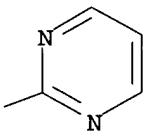
IT **477249-28-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(.alpha.v.beta.3 **integrin** receptor targeting liposome delivery system for nucleic acids)

RN 477249-28-8 CAPLUS
CN 2-Oxa-7-thia-4,8-diazadecan-10-oic acid, 3-oxo-1-phenyl-9-[[[4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]methyl]-, 7,7-dioxide, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





L4 ANSWER 10 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:927194 CAPLUS
DOCUMENT NUMBER: 138:8422
TITLE: **Integrin**-specific targeted multivalent macromolecules
INVENTOR(S): Danthi, Narasimhan S.; Choi, Steven H.; Bednarski, Mark David; Wartchow, Charles Aaron; Dechene, Neal Edward; Pease, John S.; Shen, Zhi Min; Zhang, Michael; Trulson, Julie
PATENT ASSIGNEE(S): Targesome, Inc., USA
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096367	A2	20021205	WO 2002-US17191	20020530
WO 2002096367	A3	20030306		

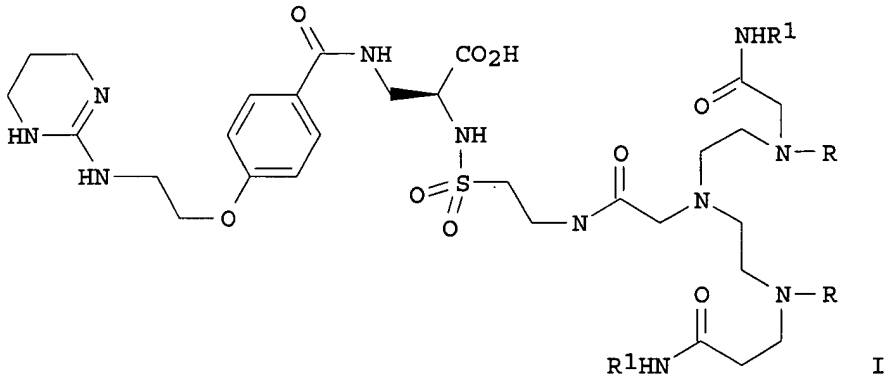
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002071843	A1	20020613	US 2001-976254	20011011

PRIORITY APPLN. INFO.:

US 2001-294309P	P	20010530
US 2001-309104P	P	20010731
US 2001-312435P	P	20010815
US 2001-976254	A	20011011
US 2000-239684P	P	20001011

GI



I

AB Targeted macromols. comprising a linking carrier and more than one targeting entity are provided, as well as methods for their prepn. and use. Targeted therapeutic agents, comprising a linking carrier, a therapeutic entity assocd. with the linking carrier, and at least one targeting entity are also provided, as well as methods for their prepn. and use. E.g., I [R = CH2CONH(CH2CH2O)2CH2CH2NHCO(CH2)8C.tplbond.CC.tplbond.C(CH2)11CH3], a lipid chelator conjugated to an **integrin** agonist, was prepd. and paramagnetic polymd. nanoparticles were prepd. from I and other similar mols.

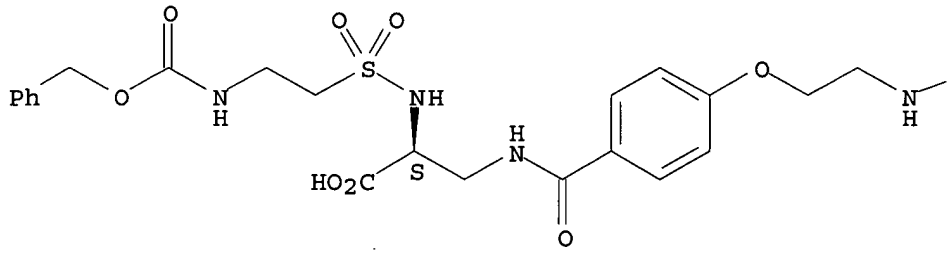
IT **477249-28-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**integrin**-specific targeted multivalent macromols.)

RN 477249-28-8 CAPLUS

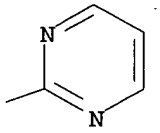
CN 2-Oxa-7-thia-4,8-diazadecan-10-oic acid, 3-oxo-1-phenyl-9-[[[4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]methyl]-, 7,7-dioxide, (9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L4 ANSWER 11 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:736230 CAPLUS

09/ 916,977

DOCUMENT NUMBER: 137:263060
TITLE: Preparation of heterocyclic compounds as .alpha.v.beta.3 **integrin** inhibitors
INVENTOR(S): Morie, Toshiya; Iwama, Seiji; Notake, Mitsue; Kitano, Tomoko
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002074743	A1	20020926	WO 2002-JP2391	20020314

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

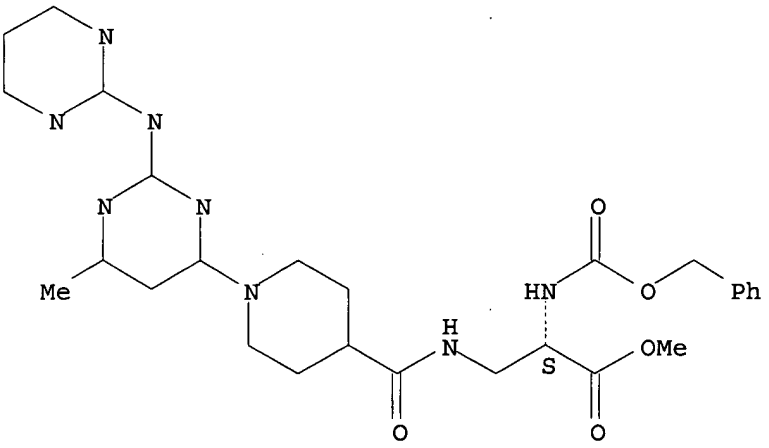
PRIORITY APPLN. INFO.: JP 2001-79029 A 20010319
OTHER SOURCE(S): MARPAT 137:263060

AB The title compds. UN(R3)ABZCH(R5)CH(R6)CO2R7 [U represents 1,4,5,6-tetrahydropyrimidine-2-yl group or the like, A represents a phenylene group or the like, B represents piperidine-1,4-diyl group or the like, Z represents CONH or the like, R3 represents hydrogen or the like, R5 represents hydrogen, an aryl group or the like, R6 represents a monosubstituted amino group, such as a benzyloxycarbonyl amino group, or the like, and R7 represents hydrogen or the like] are prepd. In an in vitro test for .alpha.v.beta.3 **integrin** binding inhibition, compds. of this invention showed IC50 values of 0.041 nM to 5.1 nM.

IT **461719-70-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclic compds. as .alpha.v.beta.3 **integrin** inhibitors)

RN 461719-70-0 CAPLUS
CN L-Alanine, 3-[[[1-[6-methyl-2-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]-4-pyrimidinyl]-4-piperidinyl]carbonyl]amino]-N-[(phenylmethoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



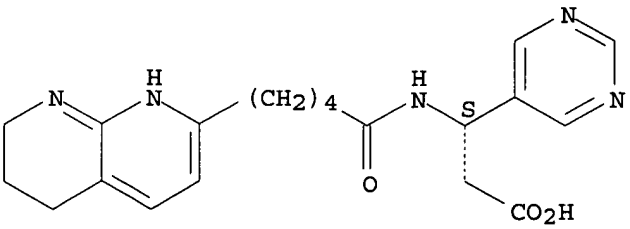
*** FRAGMENT DIAGRAM IS INCOMPLETE ***
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:585064 CAPLUS
DOCUMENT NUMBER: 138:231269
TITLE: Non-Peptide .alpha.v.beta.3 Antagonists. Part 4: Potent and Orally Bioavailable Chain-Shortened RGD Mimetics
AUTHOR(S): Coleman, Paul J.; Askew, Ben C.; Hutchinson, John H.; Whitman, David B.; Perkins, James J.; Hartman, George D.; Rodan, Gideon A.; Leu, Chih-Tai; Prueksaritanont, Thomayant; Fernandez-Metzler, Carmen; Merkle, Kara M.; Lynch, Robert; Lynch, Joseph J.; Rodan, Sevgi B.; Duggan, Mark E.
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(17), 2463-2465
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:231269

AB Potent non-peptidic .alpha.v.beta.3 antagonists have been prepd. where deletion of an amide bond from an earlier series of linear RGD-mimetics provides a novel series of chain-shortened .alpha.v.beta.3 antagonists with significantly improved oral pharmacokinetics. These chain-shortened .alpha.v.beta.3 antagonists represent structurally novel **integrin** inhibitors.

IT **502160-22-7P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and structure-activity relationship of non-peptide .alpha.v.beta.3 antagonists with improved pharmacokinetics and bioavailability)
RN 502160-22-7 CAPLUS
CN 5-Pyrimidinepropanoic acid, .beta.-[[1-oxo-5-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)pentyl]amino]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:409266 CAPLUS
DOCUMENT NUMBER: 136:409377
TITLE: Preparation of amine salts of an **integrin** receptor antagonist
INVENTOR(S): Humphrey, Guy R.; Waters, Marjorie See; Xu, Wei
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002065291	A1	20020530	US 2001-998416	20011129
US 6444680	B2	20020903		

PRIORITY APPLN. INFO.: US 2000-250268P P 20001130

AB Amine salts of 3-(2-methyl-pyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-[1,8]-naphthyridin-2-yl)nonanoic acid are potent antagonists of the **integrin** .alpha.v.beta.3 receptor and are useful for the prevention and/or treatment of osteoporosis and vascular restenosis, as well as conditions assocd. with excessive angiogenesis, such as macular degeneration, diabetic retinopathy, atherosclerosis, inflammatory arthritis, cancer, and metastatic tumor growth. The invention also relates to a process for the prepn. of the novel salts as well as pharmaceutical compns. contg. the salts and methods of using the salts. Also disclosed are 3(R)- and 3(S)-(2-methylpyrimidin-5-yl)-9-(5,6,7,8-tetrahydro-[1,8]naphthyridin-2-yl)nonanoic acid (I) in the form of a zwitterion trihydrate. Thus, I were prepd. in a series of steps. A 100-mg tablet was composed of 100 mg active ingredient, 276 mg mannitol, 20 mg of croscarmellose sodium, and 4 mg magnesium stearate.

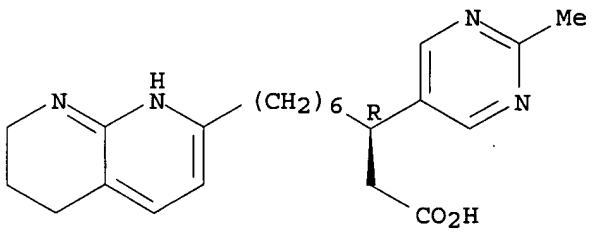
IT **431040-45-8P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amine salts of **integrin** receptor antagonist)

RN 431040-45-8 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-, (.beta.R)-, compd. with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (9CI) (CA INDEX NAME)

CM 1

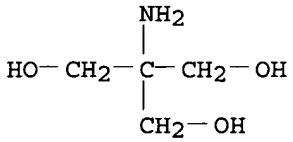
CRN 227753-48-2
CMF C22 H30 N4 O2

Absolute stereochemistry.



CM 2

CRN 77-86-1
CMF C4 H11 N O3



L4 ANSWER 14 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:349146 CAPLUS
DOCUMENT NUMBER: 136:369608
TITLE: Preparation of 3-(N'-oxodihydropyridinylureido)-3-phenylpropanoates as inhibitors of .alpha.4.beta.1 **integrin** binding
INVENTOR(S): Biediger, Ronald J.; Chen, Qi; Holland, George W.; Kassir, Jamal M.; Li, Wen; Market, Robert V.; Scott, Ian L.; Wu, Chengde; Decker, Radford E.; Li, Jian
PATENT ASSIGNEE(S): Texas Biotechnology Corporation, USA
SOURCE: Eur. Pat. Appl., 131 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1203766	A2	20020508	EP 2001-125494	20011106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2001005394	A	20020507	NO 2001-5394	20011105
CN 1412181	A	20030423	CN 2001-145182	20011229
JP 2003119181	A2	20030423	JP 2002-31953	20020208

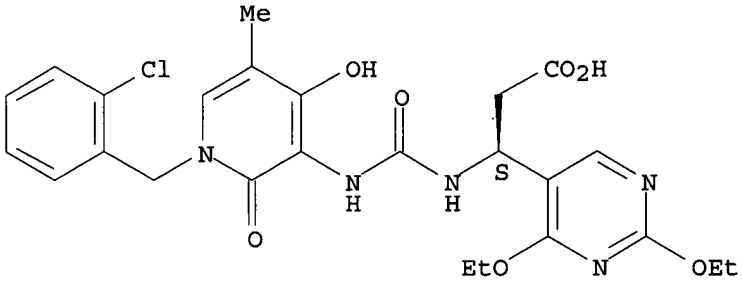
PRIORITY APPLN. INFO.: US 2000-707068 A 20001106
US 2001-973142 A 20011009
OTHER SOURCE(S): MARPAT 136:369608
AB Title compds. were prepd. Thus, 2-ClC6H4CH2ZNH2 (Z = 4-ethyl-2-oxo-1,2-dihydropyridine-1,3-diyl)(prepn. given) was condensed with (S)-4-MeC6H4CH(NH2)CH2CO2Et and COCl2 to give, after sapon., (S)-2-ClC6H4CH2ZNHCONHCH(C6H4Me-4)CH2CO2H (Z as above). Data for biol. activity of title compds. were given.
IT **422516-89-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 3-(N'-oxodihydropyridinylureido)-3-phenylpropanoates as inhibitors of .alpha.4.beta.1 **integrin** binding)

RN 422516-89-0 CAPLUS

CN 5-Pyrimidinepropanoic acid, .beta.-[[[[1-[(2-chlorophenyl)methyl]-1,2-dihydro-4-hydroxy-5-methyl-2-oxo-3-pyridinyl]amino]carbonyl]amino]-2,4-diethoxy-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:275794 CAPLUS

DOCUMENT NUMBER: 136:309803

TITLE: Preparation of a phosphoric acid salt of an **integrin** receptor antagonist

INVENTOR(S): Meissner, Robert S.; Xu, Wei

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

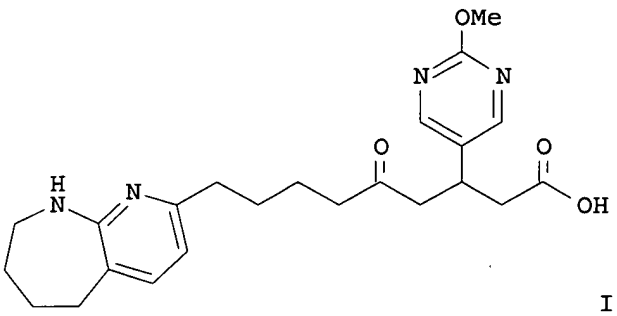
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028395	A1	20020411	WO 2001-US30647	20011001
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001096439	A5	20020415	AU 2001-96439	20011001
EP 1326615	A1	20030716	EP 2001-977309	20011001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-237534P P 20001004
WO 2001-US30647 W 20011001

GI



I

AB The phosphoric acid salt of 3-(2-methoxy-pyrimidin-5-yl)-5-oxo-9-(6,7,8,9-tetrahydro-5H-pyrido[2,3-b]azepin- -yl)-nonanoic acid (I) is a potent antagonist of the **integrin** .alpha..nu..beta.3 receptor and is useful for the prevention and/or treatment of osteoporosis and vascular restenosis, as well as conditions assocd. with excessive angiogenesis, such as macular degeneration, diabetic retinopathy, atherosclerosis, inflammatory arthritis, cancer, and metastatic tumor growth. The invention also relates to a process for the prepn. of the novel salt as well as pharmaceutical compns. and methods of use. Thus, I.cntdot.H3PO4 was prepd. from I Et ester via sapon. with aq. NaOH followed by reaction of H3PO4 in EtOH. The the crystal structure of I.cntdot.H3PO4 was detd. via x-ray powder diffraction.

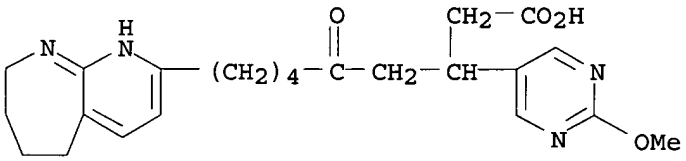
IT **408357-11-9P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of cryst. phosphoric acid salt of **integrin** .alpha..nu..beta.3 receptor antagonist useful as therapeutic for osteoporosis and vascular restenosis)

RN 408357-11-9 CAPLUS

CN 1H-Pyrido[2,3-b]azepine-2-nonanoic acid, 5,6,7,8-tetrahydro-.beta.-(2-methoxy-5-pyrimidinyl)-.delta.-oxo-, phosphate (1:1) (9CI) (CA INDEX NAME)

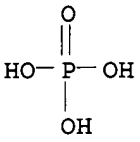
CM 1

CRN 312262-23-0
CMF C23 H30 N4 O4



CM 2

CRN 7664-38-2
CMF H3 O4 P

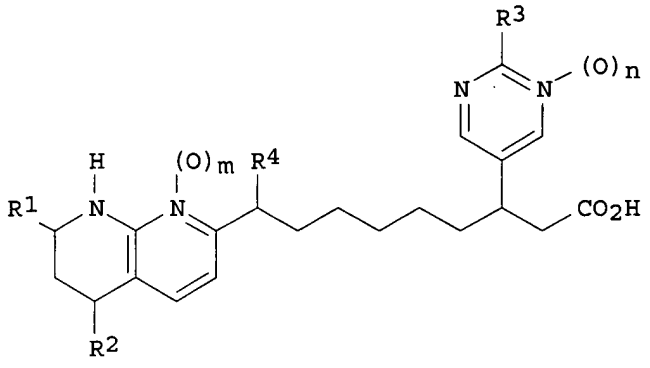


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:220592 CAPLUS
DOCUMENT NUMBER: 136:263170
TITLE: Pyrimidinylnaphthyridinenonanoic acid derivatives as .alpha.v.beta.3 **integrin** receptor antagonists
INVENTOR(S): Coleman, Paul J.; Cui, Donghui; Duggan, Mark E.; Fang, Xiaojun; Hutchinson, John H.; Prueksaritanont, Thomayant; Silva Elipe, Maria Victoria
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022616	A2	20020321	WO 2001-US28404	20010910
WO 2002022616	A3	20020606		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001090772	A5	20020326	AU 2001-90772	20010910
US 2002040030	A1	20020404	US 2001-953606	20010914

PRIORITY APPLN. INFO.: US 2000-232262P P 20000914
WO 2001-US28404 W 20010910
OTHER SOURCE(S): MARPAT 136:263170
GI



I

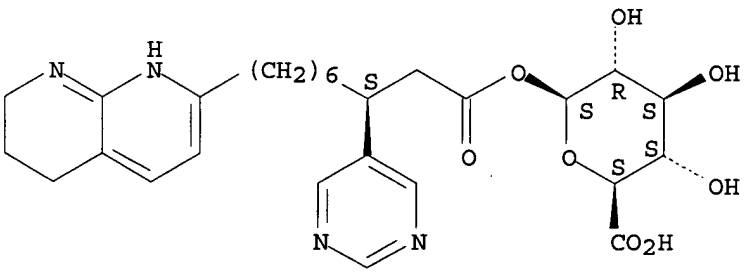
AB The title compds. I [R1, R2, R4 = H, OH, O; R3 = H, Me; m, n = 0, 1], formed by metabolic conversion of I [R1, R2, R4 = H; R3 = H, Me; m, n = 0] with rat liver microsomes, are .alpha.v.beta.3 **integrin** receptor antagonists. They are particularly useful for inhibiting bone resorption and for the treatment and prevention of osteoporosis. Thus, I [R1, R2, R4 = H, R3 = Me, m, n = 0] was prepd. and was incubated with rat liver microsomes for 2.5 h at 37.degree.C to yield I [R1, R4 = H, R2 = OH, R3 = Me, m, n = 0; R1 = O, OH, R2, R4 = H, R3 = Me, m, n = 0;R1, R2 = H, R3 = Me, R4 = OH, m, n = 0; R1, R2, R4 = H, R3 = Me, m = 0, n = 1; R1, R2, R4 = H, R3 = Me, m = 1, n = 0] and the 5,6,7,8-tetradehydro analog of I [R1, R2, R4 = H, R3 = Me, m, n = 0]. The products had IC50 <100nM in the SPAV3 assay.

IT **405061-24-7**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolite formed from pyrimidinylnaphthyridinenonanoic acid .alpha.v.beta.3 **integrin** receptor antagonists)

RN 405061-24-7 CAPLUS

CN .beta.-D-Glucopyranuronic acid, 1-[(.beta.S)-1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-1,8-naphthyridine-2-nonanoate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:220369 CAPLUS

DOCUMENT NUMBER: 136:241665

TITLE: Treatment of inflammation with a combination of a cyclooxygenase-2 inhibitor and an **integrin** alpha-V antagonist

INVENTOR(S): Hartman, George; Duggan, Mark; Rodan, Gideon A.; Rodan, Sevgi B.; Duong, Le T.; Kimmel, Donald B.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2

09/ 916,977

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022124	A1	20020321	WO 2001-US42146	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001095038	A5	20020326	AU 2001-95038	20010914
EP 1322311	A1	20030702	EP 2001-975746	20010914
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002040039	A1	20020404	US 2001-955379	20010918

PRIORITY APPLN. INFO.: US 2000-233609P P 20000918
WO 2001-US42146 W 20010914

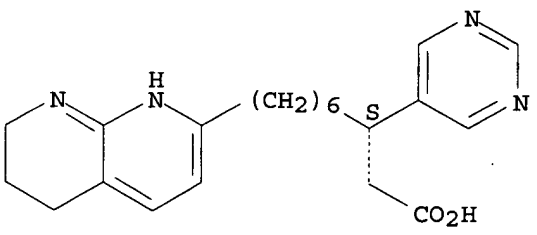
OTHER SOURCE(S): MARPAT 136:241665

AB The present invention provides for methods for treating or preventing an inflammatory disease or condition in a mammalian patient in need of such treatment comprising administering to said patient a cyclooxygenase-2 specific inhibitor in combination with an .alpha.V.beta.3, .alpha.V.beta.5, and/or .alpha.V.beta.6 **integrin** receptor antagonist in an amt. effective to treat or prevent the inflammatory disease or condition. The present invention also provides for pharmaceutical compns. for the treatment or prevention of an inflammatory disease or condition. Further, the invention provides for the manuf. of a medicament useful in the treatment or prevention of an inflammatory disease or condition.

IT **227752-24-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of inflammation with a combination of a cyclooxygenase-2 inhibitors and an **integrin**-.alpha.V antagonists)

RN 227752-24-1 CAPLUS
CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:89834 CAPLUS
DOCUMENT NUMBER: 136:134745

09/ 916,977

TITLE: Preparation of heterocycle-substituted chain-fluorinated carboxylic acids and esters useful as .alpha.v **integrin** receptor antagonists
INVENTOR(S): Wang, Jiabing
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002007730	A1	20020131	WO 2001-US22938	20010720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1315501	A1	20030604	EP 2001-955884	20010720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-220903P P 20000726
WO 2001-US22938 W 20010720

AB The present invention relates to novel chain-fluorinated alkanoic acid derivs. XCH2CH2CR32CH2CR42CH2CHR5CH2CO2R6 (1; e.g. (3S)-5,5-difluoro-3-(2-methylpyrimidin-5-yl)-9-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)nonanoic acid), their synthesis, and their use as .alpha.v **integrin** receptor antagonists. More particularly, the compds. of the present invention are antagonists of the **integrin** receptors .alpha.v.beta.3 and/or .alpha.v.beta.5 and are useful for inhibiting bone resorption, treating and preventing osteoporosis, and inhibiting vascular restenosis, diabetic retinopathy, macular degeneration, angiogenesis, atherosclerosis, inflammation, inflammatory arthritis, viral disease, cancer, and metastatic tumor growth. In 1, X = 5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl, 2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-2-yl, 5,6,7,8-tetrahydro-9H-pyrido[2,3-b]azepin-2-yl, or 6-R2NHpyridin-2-yl, wherein each nonarom. ring C atom is unsubstituted or independently substituted with one or two R1 substituents and each arom. ring C atom is unsubstituted or independently substituted with one R1 substituent. R1 = C1-8 alkyl, C3-8 cycloalkyl, C3-8 cycloheteroalkyl, C3-8 cycloalkyl-C1-6 alkyl, C3-8 cycloheteroalkyl-C1-6 alkyl, aryl, aryl-C1-6 alkyl, amino, amino-C1-6 alkyl, C1-3 acylamino, C1-3 acylamino-C1-6 alkyl, (C1-6 alkyl)1-2-amino, C3-6 cycloalkyl-C0-2 amino, (C1-6 alkyl)1-2-amino-C1-6-alkyl, C1-6 alkoxy, C1-4 alkoxy-C1-6 alkyl, hydroxycarbonyl, hydroxycarbonyl-C1-6 alkyl, C1-3 alkoxycarbonyl, C1-3 alkoxycarbonyl-C1-6 alkyl, hydroxy, hydroxy-C1-6-alkyl, nitro, cyano, trifluoromethyl, trifluoromethoxy, trifluoroethoxy, C1-8 alkyl-S(O)0-2, (C1-8 alkyl)0-2-aminocarbonyl, C1-8 alkyloxycarbonylamino, (C1-8 alkyl)1-2-aminocarbonyloxy, (aryl C1-3 alkyl)1-2-amino, (aryl)1-2-amino, aryl-C1-3 alkylsulfonylamino, and C1-8 alkylsulfonylamino; or two R1 substituents, when on the same nonarom. C atom, are taken together with the C atom to which they are attached to form a carbonyl group, or two R1 substituents, together with the nonarom. C atoms to which they are attached, join to form a 4- to 6-membered satd. or unsatd. carbocyclic ring. R2 is H or C1-4 alkyl; R3 is fluoro and R4 is H or R3 is H and R4 is fluoro. Although the methods of prepn. are not claimed, .apprx.10 example prepns. are included. Representative compds. of the present

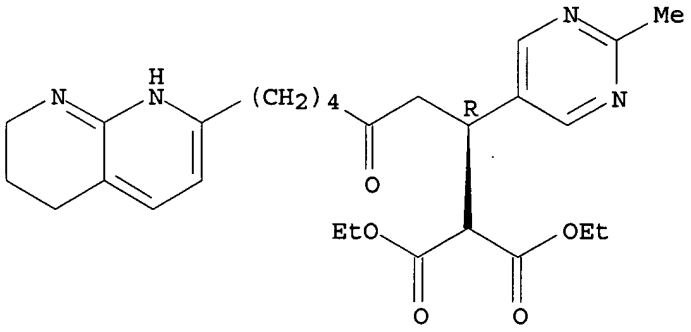
invention were tested and found to bind to human .alpha.v.beta.3 **integrin**. These compds. were generally found to have IC50 values <10 nM in the SPAV3 assay. Representative compds. of the present invention were also tested in the SPAV5 assay to det. affinity for the .alpha.v.beta.5 receptor. These compds. were generally found to have IC50 values <100 nM.

IT **312262-91-2P**, 2-[(1R)-(2-Methylpyrimidin-5-yl)-3-oxo-7-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)heptyl]malonic acid diethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of heterocycle-substituted chain-fluorinated carboxylic acids and esters useful as .alpha.v **integrin** receptor antagonists)

RN 312262-91-2 CAPLUS

CN Propanedioic acid, [(1R)-1-(2-methyl-5-pyrimidinyl)-3-oxo-7-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)heptyl]-, diethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:564868 CAPLUS
DOCUMENT NUMBER: 135:147423
TITLE: Remedies for reperfusion injury containing **integrin** .alpha.v.beta.3 antagonist
INVENTOR(S): Fujishima, Kazuyuki; Murakami, Shoichi; Yamamoto, Mikio; Abe, Mitsuhiro; Ishikawa, Minoru; Ouchi, Shokichi; Ajito, Keiichi
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001054726	A1	20010802	WO 2001-JP496	20010125

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001028819	A5	20010807	AU 2001-28819	20010125
EP 1250935	A1	20021023	EP 2001-946792	20010125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003040531	A1	20030227	US 2002-182035	20020725

PRIORITY APPLN. INFO.: JP 2000-16342 A 20000125
WO 2001-JP496 W 20010125

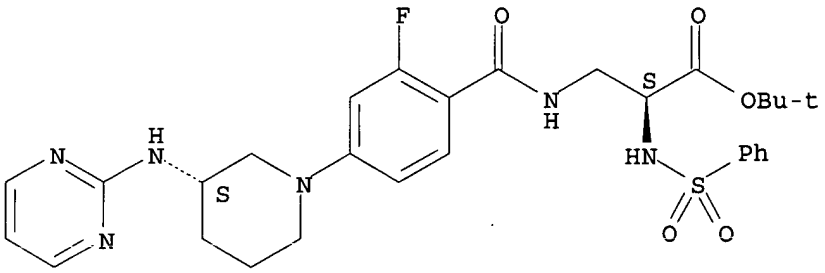
AB Drugs by which reperfusion injury can be clin. efficiently prevented or treated. These remedies or preventives for reperfusion injury contain as the active ingredient an **integrin** .alpha.v.beta.3 antagonist, pharmaceutically acceptable salts thereof or solvates of the same.

IT **334619-04-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(remedies for reperfusion injury contg. **integrin** .alpha.v.beta.3 antagonist)

RN 334619-04-4 CAPLUS

CN L-Alanine, 3-[[2-fluoro-4-[(3S)-3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



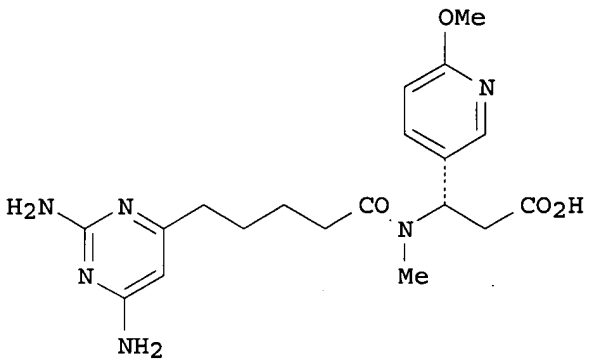
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:545664 CAPLUS
DOCUMENT NUMBER: 135:137514
TITLE: Preparation and formulation heterocyclyl-alkanoic acids for pharmaceutical use as **integrin** .alpha.v receptor antagonists
INVENTOR(S): Askew, Ben C.; Breslin, Michael J.; Duggan, Mark E.; Hutchinson, John H.; Meissner, Robert S.; Perkins, James J.; Steele, Thomas G.; Patane, Michael A.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053262	A1	20010726	WO 2001-US1953	20010119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU,				

LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,
SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1254116 A1 20021106 EP 2001-908643 20010119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003520271 T2 20030702 JP 2001-553266 20010119
US 2001053853 A1 20011220 US 2001-767471 20010123
PRIORITY APPLN. INFO.: US 2000-177792P P 20000124
US 2000-230469P P 20000906
WO 2001-US1953 W 20010119
OTHER SOURCE(S): MARPAT 135:137514
GI



I

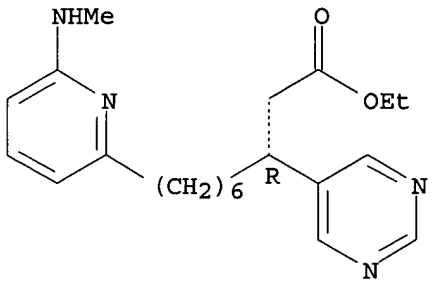
AB Heterocyclyl-alkanoic acids, such as X-(CH2)4-Y-CHR4CH2CO2R5 [X = nitrogen contg. heterocyclyl, such as pyridinyl, pyrimidinyl, azaindolyl, etc.; Y = (CH2)2, CONR3; R3, R5 = H, alkyl; R4 = aryl or heteroaryl, such as Ph, naphthyl, furyl thienyl, imidazolyl, etc.] were prepd. as antagonists of the **integrin** receptors .alpha.v.beta.3 and/or .alpha..beta.5 and may be useful for inhibiting bone resorption, treating and preventing osteoporosis, and inhibiting vascular restenosis, diabetic retinopathy, macular degeneration, angiogenesis, atherosclerosis, inflammatory arthritis, cancer, and metastatic tumor growth. Thus, the trifluoroacetic acid salt of heterocyclyl-alkanoic acid I was prepd. via a multistep synthetic sequence starting from 2-methoxypyridine, Et acrylate, Et 4-pentenoate, and 6-chloro-2,4-diaminopyrimidine. The prepd. acids were tested for **integrin** .alpha.v.beta.3 and .alpha..beta.5 binding activity and bone resorption activity. Examples of pharmaceutical formulations of the heterocyclyl-alkanoic acids were also presented.

IT **351447-25-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. and formulation heterocyclyl-alkanoic acids for pharmaceutical use as **integrin** .alpha.v receptor antagonists)

RN 351447-25-1 CAPLUS

CN 5-Pyrimidinepropanoic acid, .beta.-[6-[6-(methylamino)-2-pyridinyl]hexyl]-, ethyl ester, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

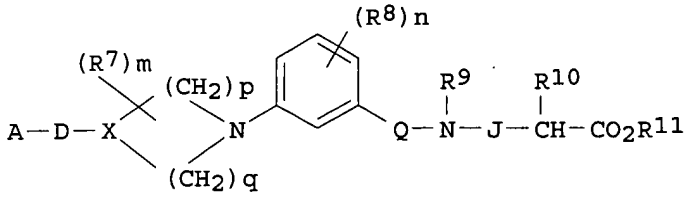


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:283934 CAPLUS
DOCUMENT NUMBER: 134:295835
TITLE: Preparation of m-substituted benzoic acid derivatives exhibiting **integrin** .alpha.v.beta.3 antagonism
INVENTOR(S): Ajito, Keiichi; Ishikawa, Minoru; Kubota, Dai; Murakami, Shoichi; Yamamoto, Mikio; Yahata, Naokazu; Fujishima, Kazuyuki; Oyama, Makoto
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 172 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027090	A1	20010419	WO 2000-JP7031	20001010
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000075599	A5	20010423	AU 2000-75599	20001010
EP 1229024	A1	20020807	EP 2000-964758	20001010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: JP 1999-288487 A 19991008
WO 2000-JP7031 W 20001010
OTHER SOURCE(S): MARPAT 134:295835
GI



I

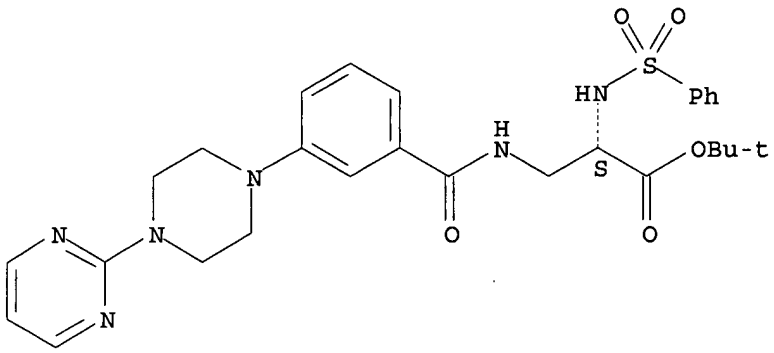
AB M-Substituted benzoic acid derivs. represented by general formula [I; A = (un)substituted H2NC(:NH), optionally substituted (un)satd. 5- to 7-membered ring heterocyclyl contg. 2 N atoms optionally condensed with other 5- to 7-membered ring carbocyclic or heterocyclic rin to form an (un)substituted bicyclic ring; D = single bond, (un)substituted NH; X = CH, N; R7, R8 = (un)substituted C1-6 alkyl or alkoxy, halo, NH2, NO2, cyano, OH, SH, C1-4 alkyl thio, phenylthio, O; Q = CO, CH2, C1-6 alkyl-CH; R9 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, or aralkyl; J = single bond, (un)substituted C1-3 alkylene; R10 = H, (un)substituted HO, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, aralkyl, or NH2; R11 = H, (un)substituted aralkyl or C1-6 alkyl; m = 0-5; n = 0-4; p, q = 0-3], which improve **integrin** .alpha.v.beta.3 antagonism over **integrin** .alpha.11b.beta.3 antagonism and water soly., are prepd. These compds. also exhibit glycoprotein IIb/IIIa antagonism and cell adhesion-inhibitory and blood platelet aggregation-inhibitory activity. These derivs. are useful in the treatment or prevention of cardiovascular diseases, vascularization-related diseases, cerebrovascular diseases, cancers and metastases thereof, immunol. diseases, bone diseases, and so on. Thus, (2S)-(+)-Benzenesulfonylamino-3-[3-{4-(pyrimidin-2-yl)piperazin-1-yl}benzoylamino]propionic acid (prepn. given) was hydrogenated over 10% Pd/C in a mixt. of 1,4-dioxane, acetic acid, and 1 N aq. HCl under hydrogen atm. with stirring for 5 h to give (2S)-(+)-Benzenesulfonylamino-3-[3-{4-(1,4,5,6-tetrahydropyrimidin-2-yl)piperazin-1-yl}benzoylamino]propionic acid (II). II in vitro exhibited **integrin** .alpha.v.beta.3 antagonism and glycoprotein IIb/IIIa antagonism with IC50 of 1.3 and 2.0 nM, resp.

IT **334792-09-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of m-substituted benzoic acid derivs. as **integrin** .alpha.v.beta.3 antagonists and therapeutics)

RN 334792-09-5 CAPLUS

CN L-Alanine, N-(phenylsulfonyl)-3-[[3-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

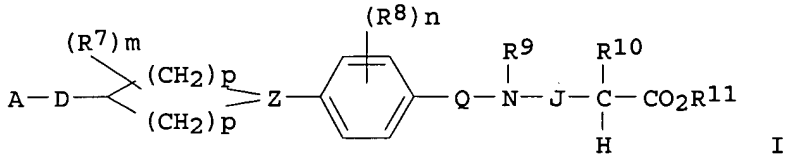


REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:283926 CAPLUS
DOCUMENT NUMBER: 134:295833
TITLE: Preparation of 3-aminopiperidine derivatives as **integrin** .alpha.v.beta.3 antagonists
INVENTOR(S): Ishikawa, Minoru; Kubota, Dai; Hiraiwa, Yukiko; Tsushima, Masaki; Yamamoto, Mikio; Yahata, Naokazu; Kuroda, Chizuko; Abe, Mitsuhiro; Fujishima, Kazuyuki; Murakami, Shoichi; Ajito, Keiichi
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 167 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027082	A1	20010419	WO 2000-JP7033	20001010
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000075601	A5	20010423	AU 2000-75601	20001010
EP 1227083	A1	20020731	EP 2000-964760	20001010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: JP 1999-288904 A 19991008
WO 2000-JP7033 W 20001010
OTHER SOURCE(S): MARPAT 134:295833
GI



I

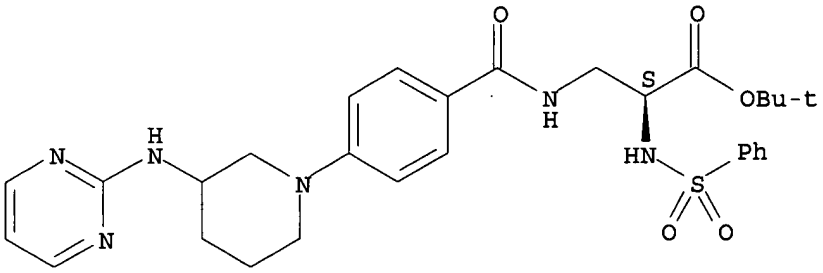
AB Compds. represented by general formula [I; A = (un)substituted C(:NH)NH2, C(:CH2)NH2, or heterocyclic group contg. at least one nitrogen atom; D = (un)substituted NH, O, S, or NHCH2; Z = CH, N; R7, R8 = (un)substituted C1-6 alkyl or alkoxy, halo, NH2, NO2, OH, O; Q = CO, CH2, C1-6 alkyl-CH, CHOH, (C1-6 alkoxy)-CH; R9 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, or aralkyl; J = single bond, (un)substituted C1-3 alkylene; R10 = H, OH, C1-6 alkoxy, (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, aralkyl, or NH2; R11 = H, C1-6 optionally substituted by 1 or 2 Ph groups; m = 0-5; n = 0-4; p = 3,4; q = 0-3], wherein basic groups are attached to the 3-position of piperidine ring either directly or via various groups, are prepd. These compds. are useful for treating **integrin** .alpha.v.beta.3-mediated diseases or diseases for which cell adhesion-inhibitory, GP IIb/IIIa antagonism and/or blood platelet aggregation-inhibitory activity is effective and in particular are useful in treating or preventing cardiovascular diseases, diseases in assocn. with angiogenesis, cerebrovascular diseases, cancer and metastasis thereof, immune diseases, and bone diseases. Thus, 3-fluoro-4-[(3S)-3-(pyrimidin-2-ylamino)piperidin-1-yl]benzoic acid was condensed with (2S)-N-benzenesulfonyl-2,3-diaminopropanoic acid using 1-hydroxybenzotriazole, N-methylmorpholine, and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in DMF at room temp. for 10 h to give (2S)-2-(benzenesulfonylamino)-3-[3-fluoro-4-[(3S)-3-(pyrimidin-2-ylamino)piperidin-1-yl]benzoylamino]propanoic acid tert-Bu ester which was treated with CF3CO2H in CH2Cl2 at room temp. for 20 h to give (2S)-2-(benzenesulfonylamino)-3-[3-fluoro-4-[(3S)-3-(pyrimidin-2-ylamino)piperidin-1-yl]benzoylamino]propanoic acid trifluoroacetate. The latter compd. was hydrogenated over 10% Pd-C in aq. dioxane at room temp. for 4 h to give, after chromatog. purifn., (2S)-2-(benzenesulfonylamino)-3-[3-fluoro-4-[(3S)-3-(1,4,5,6-tetrahydropyrimidin-2-ylamino)piperidin-1-yl]benzoylamino]propanoic acid, which.

IT **334617-98-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 3-aminopiperidine derivs. as **integrin** .alpha.v.beta.3 antagonists for preventives or therapeutics)

RN 334617-98-0 CAPLUS

CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[3-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

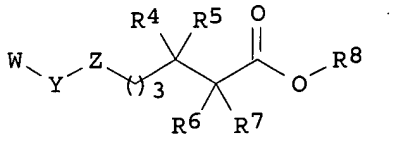


REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

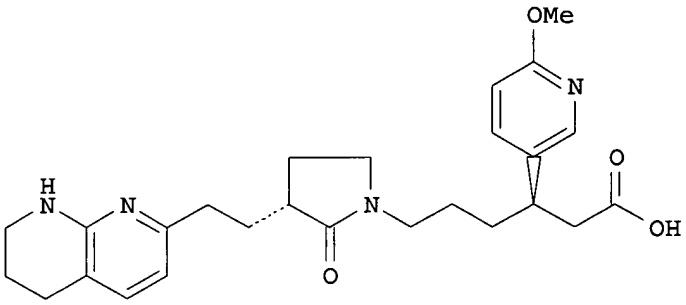
L4 ANSWER 23 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:265252 CAPLUS
DOCUMENT NUMBER: 134:295810
TITLE: Synthesis and use of substituted pyrrolidin-1-yl hexanoic acid derivatives as .alpha..nu..beta.3 and .alpha..nu..beta.5 **integrin** receptors
INVENTOR(S): Askew, Ben C.; Smith, Garry R.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001024797	A1	20010412	WO 2000-US27033	20000929
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1229910	A1	20020814	EP 2000-967201	20000929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003510360	T2	20030318	JP 2001-527796	20000929
US 6413955	B1	20020702	US 2000-677677	20001002

PRIORITY APPLN. INFO.: US 1999-157490P P 19991004
WO 2000-US27033 W 20000929
OTHER SOURCE(S): MARPAT 134:295810
GI



I



II

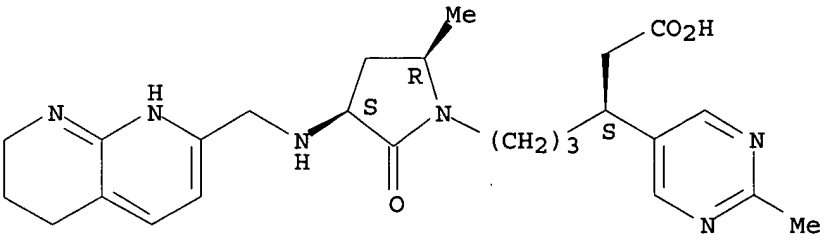
AB Compds. of formula I [wherein; W is a 5 or 6 membered monocyclic (arom.) ring having 1-4 heteroatoms (N, O or S) wherein the ring nitrogen atoms are unsubstituted or substituted with 1 or 2 R1 groups, or a 9-14 membered polycyclic ring system, wherein the polycyclic ring system has 1-4 heteroatoms (N, O or S) in which the N atoms are substituted as described above; Y is (CH2)m, (CH2)m-(O, NR2 or S(O)0-2)-(CH2)n, etc., where any CH2 can be substituted with 1 or 2 R3 groups, m is 0-3 and n is 0-3; Z is a 5-6 membered heterocyclic system having 1-3 heteroatoms (N, O or S) optionally substituted with one or more R9 group and when 2 R9 substituents are on the same C-atom, they are taken together to form a C3-C6 cycloalkyl group; R1 is H, halo, (cyclo)alkyl, cycloheteroalkyl, aryl(alkyl), amino(alkyl), etc.; R2 is H, alkyl, aryl(alkyl), aminocarbonyl, cycloalkyl, aminoalkyl, etc.; R3 is H, alkyl, aryl(alkyl), halo, OH, oxo, CF3, etc.; R4 and R5 are H, alkyl, aryl(alkyl), halo, OH, alkylcarbonylamino, etc. or taken together the C-atom to form a CO; R6 and R7 are H, alkyl, aryl(alkyl), halo, OH, etc.; R8 is H, alkyl, aryl(alkyl), alkylcarbonyloxyalkyl, etc.; R9 is H, alkyl, aryl, halo, OH, etc.;]. Several examples of I are provided. For instance II was synthesized in 14 steps as a single enantiomer. Compds. I are antagonists of the **integrin** receptors .alpha..nu..beta.3 and/or .alpha..nu..beta.5. Compds. I were found to bind to human .alpha..nu..beta.3 **integrin** with IC50 values less than 10 nM and to the .alpha..nu..beta.5 **integrin** receptor with IC50 values less than 100 nM in competitive binding assays. A bone resorption-pit assay demonstrated the ability of compds. I to inhibit osteoclasts (bovine bone slices). Claimed uses for I are for inhibiting bone resorption, treating and preventing osteoporosis, inhibiting vascular restenosis, diabetic retinopathy, macular degeneration, angiogenesis, atherosclerosis, inflammatory arthritis, cancer, and metastatic tumor growth.

IT **334009-69-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and use of substituted pyrrolidin-1-yl hexanoic acid derivs. as .alpha..nu..beta.3 and .alpha..nu..beta.5 **int grin** receptor antagonists)

RN 334009-69-7 CAPLUS

CN 5-Pyrimidinepropanoic acid, 2-methyl-.beta.-[3-[(3S,5R)-5-methyl-2-oxo-3-[[(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)methyl]amino]-1-pyrrolidinyl]propyl]-, (.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



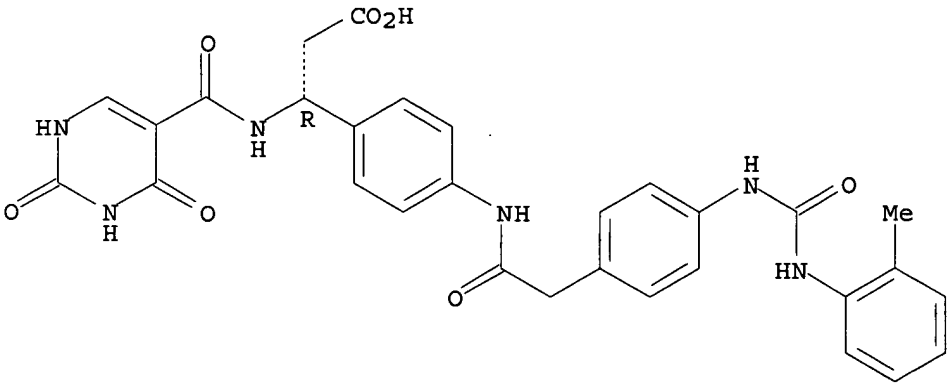
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:237851 CAPLUS
DOCUMENT NUMBER: 134:252261
TITLE: Preparation of heterocyclylcarbonylamino-modified phenylpropanes and their use as **integrin** VLA-4 binding inhibitors
INVENTOR(S): Yokota, Masaki; Nagashima, Shinya; Sugane, Takashi; Igarashi, Susumu; Moridaira, Koichiro; Miura, Ayanori; Ikeda, Masaru; Takeuchi, Makoto
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001089448	A2	20010403	JP 1999-271096	19990924

PRIORITY APPLN. INFO.: JP 1999-271096 19990924
OTHER SOURCE(S): MARPAT 134:252261
AB 4-RcCH2CONRdC6H4CH(NReCORb)CH2CO2Ra [Ra = H, ester residue (prodrug); Rb = morpholino, 2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl; Rc = (un)substituted (hetero)aryl; Rd, Re = H, lower alky], useful for treatment of asthma, allergy, rheumatoid arthritis, autoimmune disease, rejection, inflammation, arteriosclerosis, cancer metastasis, diabetes, etc., are prepd. Thus, a soln. of 5-methoxyindoleacetic acid and Et (RS)-3-(4-aminophenyl)-3-[(morpholine-4-carbonyl)amino]propanoate in DMF was treated with WSC.HCl and HOBt at room temp. for 20 h to give the corresponding amide.
IT **331681-16-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclylcarbonylamino-modified phenylpropanes as **integrin** VLA-4 binding inhibitors for treatment of diseases)
RN 331681-16-4 CAPLUS
CN Benzenepropanoic acid, 4-[[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]-.beta.-[[(1,2,3,4-tetrahydro-2,4-dioxo-5-pyrimidinyl)carbonyl]amino]-, (.beta.R)- (9CI) (CA INDEX NAME)

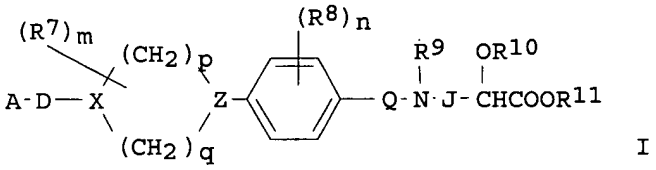
Absolute stereochemistry.



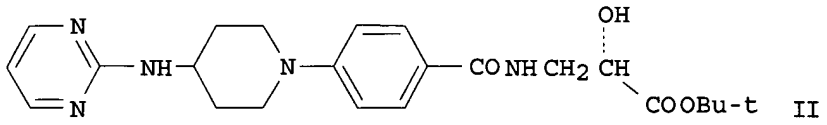
L4 ANSWER 25 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:115127 CAPLUS
DOCUMENT NUMBER: 134:163066
TITLE: Preparation and effect of .omega.-amino-.alpha.-hydroxycarboxylic acid derivatives having **integrin** .alpha.v.beta.3 antagonism
INVENTOR(S): Ajito, Keiichi; Yahata, Naokazu; Ishikawa, Minoru; Kubota, Dai; Murakami, Shoichi; Yamamoto, Mikio; Fujishima, Kazuyuki; Gomi, Shuichi; Ouchi, Shokichi
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001010844	A1	20010215	WO 2000-JP5177	20000802
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1209152	A1	20020529	EP 2000-949959	20000802
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: JP 1999-222098 A 19990805
WO 2000-JP5177 W 20000802
OTHER SOURCE(S): MARPAT 134:163066
GI



I



II

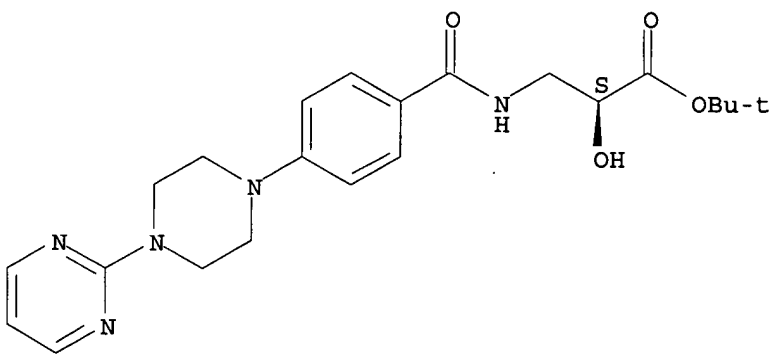
AB Title compds. [I; wherein A represents an optionally substituted 5- to 7-membered heterocyclic group contg. 2 nitrogen atoms which may be condensed with other ring(s) or C(NR2)(:NR3); D represents a bond, NR4,O or S; X and Z represent each CH or N; R7 and R8 represent each C1-6 alkyl, halogeno, oxygen, etc.; Q represents CO, CHR13 or CHOR13; J represents a bond or C1-3 alkylene; R1 to R4, R9 to R11 and R13 represent each hydrogen, alkyl, etc.; m is an integer of from 0 to 5; n is an integer of from 0 to 4; and p and q are each an integer of from 1 to 3], which are highly sol. in water and having an **integrin** .alpha.v.beta.3 antagonism, and pharmaceutical acceptable salts are prepd. Thus, the title compd. II was prepd. and tested.

IT **324781-18-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and effect of .omega.-amino-.alpha.-hydroxycarboxylic acid derivs. having **integrin** .alpha.v.beta.3 antagonism)

RN 324781-18-2 CAPLUS

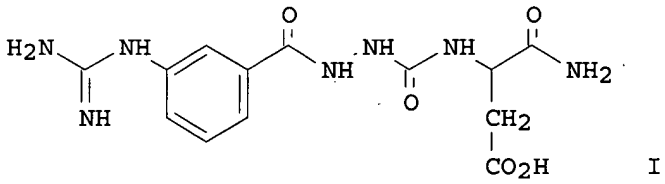
CN Propanoic acid, 2-hydroxy-3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:53692 CAPLUS
DOCUMENT NUMBER: 134:223033
TITLE: Nonpeptidic .alpha.v.beta.3 **integrin** antagonist libraries: on-bead screening and mass spectrometric identification without tagging
AUTHOR(S): Gibson, Christoph; Sulyok, Gabor A. G.; Hahn, Diane; Goodman, Simon L.; Holzemann, Gunter; Kessler, Horst
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Tech. Univ. Munchen, Garching, 85747, Germany
SOURCE: Angewandte Chemie, International Edition (2001), 40(1), 165-169
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



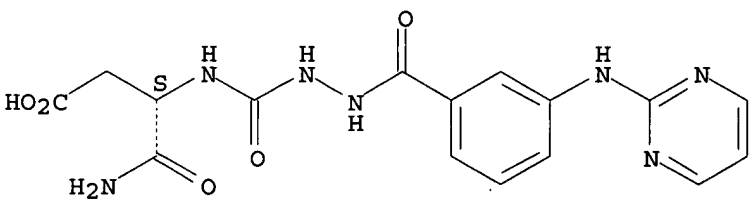
I

AB The authors report on their work for identifying low mol. wt. **integrin** ligands through application of combinatorial solid-phase synthesis, biol. on-bead evaluation, and mass spectrometric identification of selected compds., which eliminates the reduced efficiency of tagged-bead methods of synthesis. A combinatorial library of aza-RGD mimetic compds., e.g. (I), were synthesized using a split bead method, and tested for activity using a sol. .alpha.v.beta.3 **integrin** receptor system. Beads contg. active compds. were cleaved, and the active compds. identified by mass-spectra, which were unique for individual compds. due to limitations of the component selection method.

IT **329729-77-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and screening of aza-RGD mimetics using combinatorial synthesis, .alpha.v.beta.3 **integrin** recognition, and mass-spectral anal. techniques)

RN 329729-77-3 CAPLUS
CN Benzoic acid, 3-(2-pyrimidinylamino)-, 2-[[[(1S)-2-amino-1-(carboxymethyl)-2-oxoethyl]amino]carbonyl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

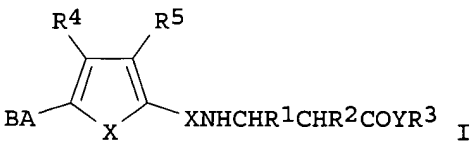


REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:881139 CAPLUS
DOCUMENT NUMBER: 134:42055
TITLE: Preparation of thiophene **integrin** inhibitors
INVENTOR(S): Labrecque, Denis; Attardo, Giorgio; Bubenik, Monica; Chan, Laval; Charron, Sylvie; Denis, Real; Falardeau, Guy; Lamothe, Serge; Preville, Patrice; Zacharie, Boulos; Rej, Rabindra
PATENT ASSIGNEE(S): Biochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075129	A1	20001214	WO 2000-CA680	20000607
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6274620	B1	20010814	US 2000-588574	20000607
EP 1187825	A1	20020320	EP 2000-938386	20000607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-137726P P 19990607
WO 2000-CA680 W 20000607
OTHER SOURCE(S): MARPAT 134:42055
GI



I

AB The title compds. I [X = O, S; W = CO, SO2; R1, R2 = H, aryl, arylsulfonylamino, etc.; R3 = H, alkyl, alkoxy, etc.; R4, R5 = H, halo, alkyl, alkoxy; A = alkyl, alkenyl, alkynyl, aryl, cycloalkyl; B = amino,aminoalkyl, guanidino, etc.], inhibitors of **integrins**, particularly .alpha.v.beta.3 and .alpha.v.beta.5 **integrins**, were prepd. E.g., 2-benzenesulfonylamino-3-{[5-(3-guanidinomethylphenyl)thiophene-2-carbonyl]amino}propionic acid trifluoroacetic acid salt was prepd.

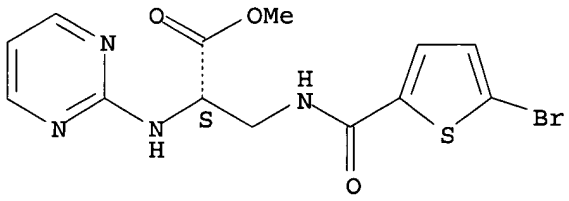
IT **312760-31-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of thiophene **integrin** inhibitors)

RN 312760-31-9 CAPLUS

09/ 916,977

CN L-Alanine, 3-[[(5-bromo-2-thienyl)carbonyl]amino]-N-2-pyrimidinyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



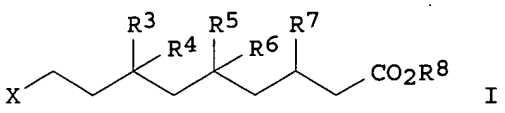
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:861451 CAPLUS
DOCUMENT NUMBER: 134:29136
TITLE: Novel nonanoic acid derivatives as alpha V **integrin** receptor antagonists
INVENTOR(S): Coleman, Paul J.; Duggan, Mark E.; Halczenko, Wasyl; Hartman, George D.; Hutchinson, John H.; Meissner, Robert S.; Patane, Michael A.; Perkins, James J.; Wang, Jiabing; Breslin, Michael J.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 166 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

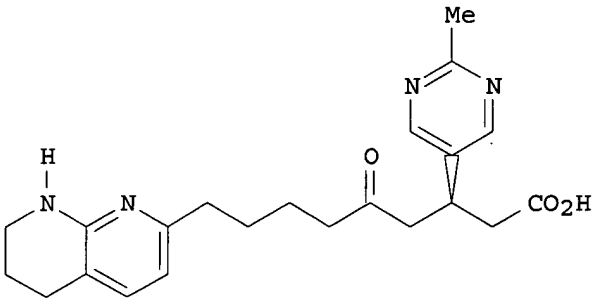
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072801	A2	20001207	WO 2000-US14901	20000530
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000011108	A	20020319	BR 2000-11108	20000530
EP 1187592	A2	20020320	EP 2000-942652	20000530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 749351	B2	20020627	AU 2000-57246	20000530
EE 200100642	A	20030217	EE 2001-642	20000530
US 6410526	B1	20020625	US 2000-583522	20000531
NO 2001005858	A	20020204	NO 2001-5858	20011130
BG 106232	A	20020628	BG 2001-106232	20011218

PRIORITY APPLN. INFO.: US 1999-137101P P 19990602
US 2000-179216P P 20000131
WO 2000-US14901 W 20000530

OTHER SOURCE(S): MARPAT 134:29136
GI



I



II

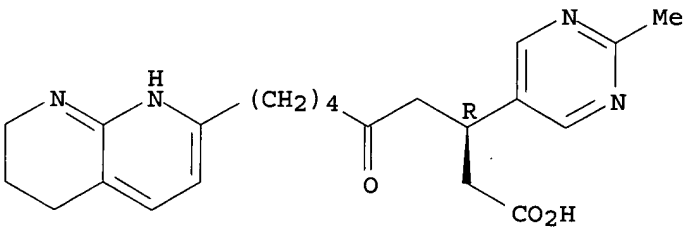
AB The invention discloses novel nonanoic acid derivs. I [X = substituted pyridine, pyrimidine, naphthyridine, etc; R3, R5 = H, OH, alkoxy; R4, R6 = H, alkyl; R3 and R4 or R5 and R6 taken together may form carbonyl oxygen; R7 = (un)substituted Ph, naphthyl, pyridyl, furyl, thienyl, etc.; R8 = H, alkyl] as .alpha.V **integrin** receptor antagonists along with methods for prepn. Thus, compd. II was prepd. in eight steps from 6-oxo-heptanoic acid with chromatog. resoln. of intermediate diketoester racemate. More particularly, the compds. of the present invention are antagonists of the **integrin** receptors .alpha.v.beta.3 and .alpha.v.beta.5, and are useful for inhibiting bone resorption, treating and preventing osteoporosis, and inhibiting vascular restenosis, diabetic retinopathy, macular degeneration, angiogenesis, atherosclerosis, inflammation, inflammatory arthritis, viral disease, cancer, and metastatic tumor growth.

IT **312261-73-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and biol. activity of nonanoic acid derivs. as .alpha.V **integrin** receptor antagonists)

RN 312261-73-7 CAPLUS

CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-(2-methyl-5-pyrimidinyl)-.delta.-oxo-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 29 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:592698 CAPLUS

DOCUMENT NUMBER: 133:164332

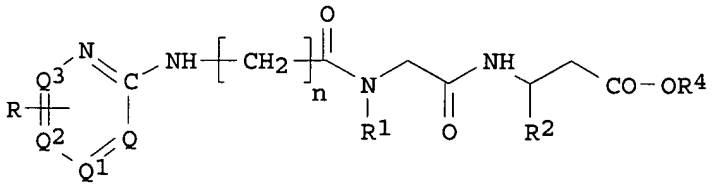
TITLE: Preparation of .beta.-alanine derivatives for use as **integrin** inhibitors

09/ 916,977

INVENTOR(S): Holzemann, Gunter; Goodman, Simon; Jonczyk, Alfred; Stahle, Wolfgang
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000048996	A2	20000824	WO 2000-EP969	20000208
WO 2000048996	A3	20001116		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1153014	A2	20011114	EP 2000-909151	20000208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008310	A	20020122	BR 2000-8310	20000208
JP 2002537287	T2	20021105	JP 2000-599737	20000208
AU 760246	B2	20030508	AU 2000-31534	20000208
NO 2001004010	A	20011018	NO 2001-4010	20010817
US 6576637	B1	20030610	US 2001-913933	20010820
ZA 2001007737	A	20021219	ZA 2001-7737	20010919

PRIORITY APPLN. INFO.: DE 1999-19907370 A 19990220
DE 1999-19957787 A 19991201
WO 2000-EP969 W 20000208
OTHER SOURCE(S): MARPAT 133:164332
GI



I

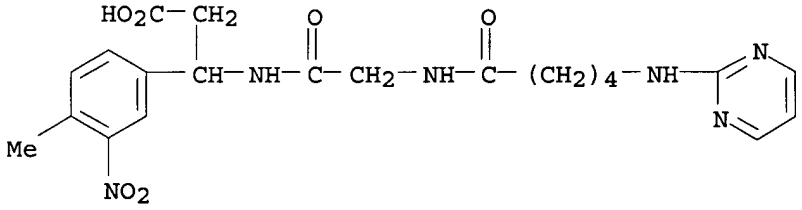
AB The invention relates to novel .beta.-alanine derivs. [(I); Q, Q1, Q2, Q3 = CH, N; R = H, alkyl, aryl, halogen, OH, alkoxy, CF3, OCF3; R1 = H, alkyl; R2 = substituted phenyl; R3 = H, alkyl, halogen, OH, alkoxy, CF3, OCF3, CN, NH2, (di)alkyl amine, alkyl amide; R4 = H, (hydroxy)alkyl, alkyl ester, (un)substituted aralkyl; n = 2-6] and to their physiol. acceptable salts or solvates, useful in the treatment of diseases as selective .alpha.v.beta.3-, .alpha.v.beta.5-, or .alpha.v.beta.6-**integrin** inhibitors. Thus, 4-(trifluoromethoxy)-benzaldehyde, malonic acid, and ammonium acetate were reacted, and the product 3-amino-3-(4-trifluoromethoxyphenyl)propionic acid was esterified with thionyl chloride and methanol to give II. Glycine Me ester was condensed with 4-(4-methylpyridin-2-ylamino)butyric acid and the deesterified product

reacted with II to give I [Q, Q1, Q2, Q3 = CH; R, R1 = H; R2 = 4-F3CO-C6H4; R4 = Me; n = 3], which was deesterified to the free propionic acid deriv. and converted to the sodium or trifluoroacetate salts. Title compds. can be used in the treatment of thrombosis, heart infarct, coronary heart diseases, arteriosclerosis, inflammations, tumors, osteoporosis, infections and restenosis after angioplasty or in pathol. processes induced or propagated by angiogenesis. Title compds. were tested for **integrin** inhibition in vivo in mice (no data).

IT **287965-36-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of .beta.-alanine derivs. for use as **integrin** inhibitors)

RN 287965-36-0 CAPLUS

CN .beta.-Alanine, N-[1-oxo-5-(2-pyrimidinylamino)pentyl]glycyl-3-(4-methyl-3-nitrophenyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:571738 CAPLUS

DOCUMENT NUMBER: 133:275850

TITLE: Nonpeptide .alpha.v.beta.3 Antagonists. 1. Transformation of a Potent, **Integrin** -Selective .alpha.IIb.beta.3 Antagonist into a Potent .alpha.v.beta.3 Antagonist

AUTHOR(S): Duggan, Mark E.; Duong, Le T.; Fisher, John E.; Hamill, Terence G.; Hoffman, William F.; Huff, Joel R.; Ihle, Nathan C.; Leu, Chih-Tai; Nagy, Rose M.; Perkins, James J.; Rodan, Sevgi B.; Wesolowski, Gregg; Whitman, David B.; Zartman, Amy E.; Rodan, Gideon A.; Hartman, George D.

CORPORATE SOURCE: Departments of Medicinal Chemistry Bone Biology and Osteoporosis Research and Pharmacology, Merck Research Laboratories, West Point, PA, 19486, USA

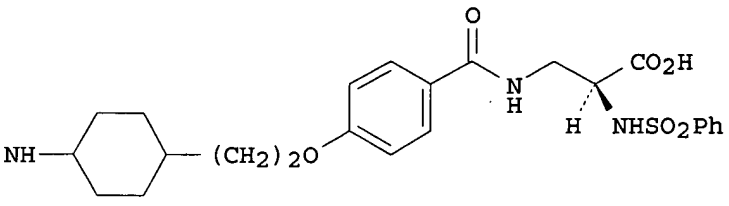
SOURCE: Journal of Medicinal Chemistry (2000), 43(20), 3736-3745
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

09/ 916,977

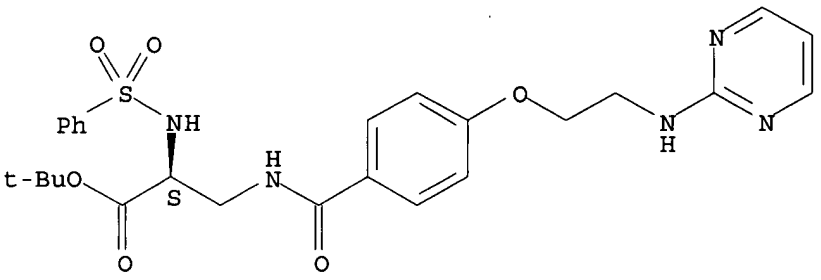
AB Modification of the potent fibrinogen receptor (.alpha.IIb.beta.3) antagonist (I) generated compds. with high affinity for the vitronectin receptor .alpha.v.beta.3. Sequential modification of the basic N-terminus of I led to the identification of the 5,6,7,8-tetrahydro[1,8]naphthyridine moiety (THN) as a lipophilic, moderately basic N-terminus that provides mols. with excellent potency and selectivity for the **integrin** receptor .alpha.v.beta.3. The THN-contg. analog is a potent inhibitor of bone resorption in vitro and in vivo. In addn., the identification of a novel, nonpeptide radioligand with high affinity to .alpha.v.beta.3 is also reported.

IT **174665-29-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of nonpeptide .alpha.v.beta.3 antagonists and transformation of **integrin**-selective .alpha.IIb.beta.3 antagonist into a potent .alpha.v.beta.3 antagonist)

RN 174665-29-3 CAPLUS

CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:260225 CAPLUS
DOCUMENT NUMBER: 132:294010
TITLE: Preparation of diaminopropionic acid derivatives as intracellular adhesion molecule-1 (ICAM-1) binding inhibitors
INVENTOR(S): Fotouhi, Nader; Gillespie, Paul; Guthrie, Robert William; Pietranico-Cole, Sherrie Lynn; Yun, Weiya
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 259 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021920	A1	20000420	WO 1999-EP7620	19991012

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,

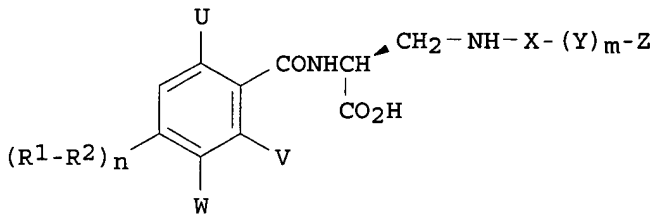
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6331640	B1	20011218	US 1999-407534	19990929
CA 2344058	AA	20000420	CA 1999-2344058	19991012
BR 9914602	A	20010703	BR 1999-14602	19991012
EP 1121342	A1	20010808	EP 1999-953772	19991012
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002527416	T2	20020827	JP 2000-575829	19991012
ZA 2001002608	A	20020930	ZA 2001-2608	20010329
US 2002052512	A1	20020502	US 2001-879700	20010612

PRIORITY APPLN. INFO.: US 1998-104120P P 19981013
US 1999-407534 A3 19990929
WO 1999-EP7620 W 19991012

OTHER SOURCE(S): MARPAT 132:294010

GI



I

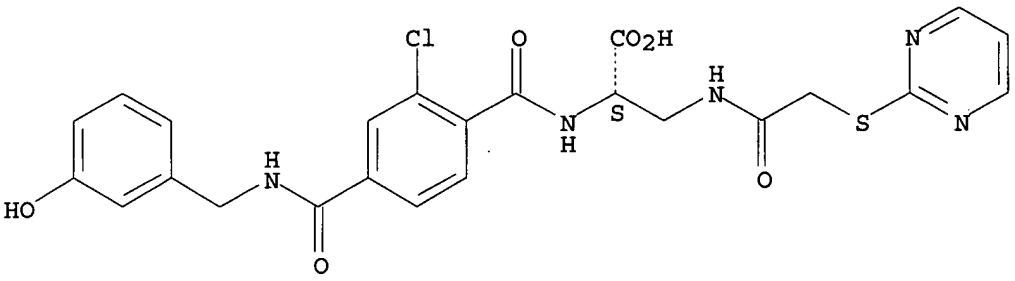
AB Diaminopropionic acid derivs. I [R1 = substituted 1-naphthyl, 4-indolyl, 4-benzimidazolyl, 4-benzodiazolyl, 4-benzotriazolyl, or phenyl; R2 = CHR3NHCO (R3 = H, carboxy, alkyl), CH2CH2CO, 1,2-cyclopropanediylcarbonyl, OCH2CO, CH:CHCHR3, CH2CH2CH(OH), CONHCHR3, or CH2NH-5,1-tetrazolediyl; U, V, W = H, halo, alkyl provided that U and V are not both hydrogen; X = CO, phenylalkylene, sulfonyl; Y = alkylene which may be substituted by amino or cycloalkyl, alkenylene, alkylenethio; Z = H, alkylthio, CO2H, CONH2, 1-adamantyl, diphenylmethyl, 3-[[(5-chloro-2-pyridinyl)amino]carbonyl]-2-pyrazinyl, hydroxy, phenylmethoxy, 2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]phenyl, [(2,6-dichlorophenyl)methoxy], Ph, (un)substituted cycloalkyl or aryl or fused ring system which may contain 0-3 heteroatoms; m, n = 0, 1] or their pharmaceutically acceptable salts or esters were prepd. and are useful for treating rheumatoid arthritis, psoriasis, multiple sclerosis, Crohn's disease, ulcerative colitis, atherosclerosis, restenosis, pancreatitis, transplant rejection, delayed graft function and diseases of ischemia reperfusion injury, including acute myocardial infarction and stroke. Thus, N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]-3-(3-methoxybenzoylamino)-L-alanine was prepd. by the solid-phase method and showed IC50 = 1.2 nM in the LFA-1 (lymphocyte function-assocd. antigen-1)/ICAM-1 protein-protein assay.

IT **264273-37-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diaminopropionic acid derivs. as intracellular adhesion mol.-1 (ICAM-1) binding inhibitors)

RN 264273-37-2 CAPLUS

CN L-Alanine, N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]-3-[[(2-pyrimidinylthio)acetyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

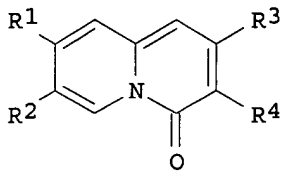


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

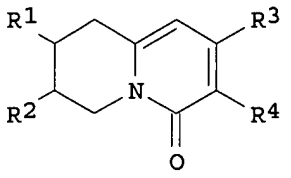
L4 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:210162 CAPLUS
DOCUMENT NUMBER: 132:237000
TITLE: Quinolizinones as **integrin** inhibitors
INVENTOR(S): Lamothe, Serge; Zacharie, Boulos; Attardo, Giorgio; Labrecque, Denis; Courchesne, Marc; Falardeau, Guy; Rej, Rabindra; Abbott, Shaun
PATENT ASSIGNEE(S): Biochem Pharma, Inc., Can.
SOURCE: PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017197	A1	20000330	WO 1999-IB1564	19990921
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9959916	A1	20000410	AU 1999-59916	19990921
EP 1115724	A1	20010718	EP 1999-969413	19990921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

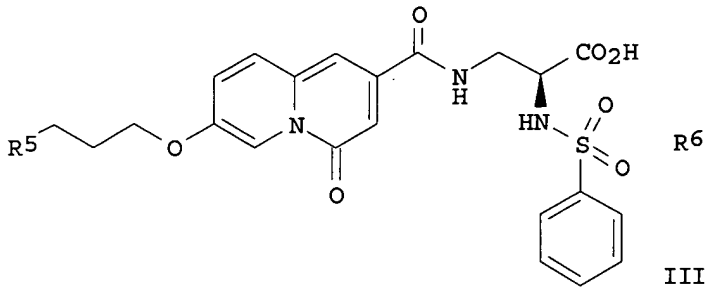
PRIORITY APPLN. INFO.: US 1998-101257P P 19980921
WO 1999-IB1564 W 19990921
OTHER SOURCE(S): MARPAT 132:237000
GI



I



II



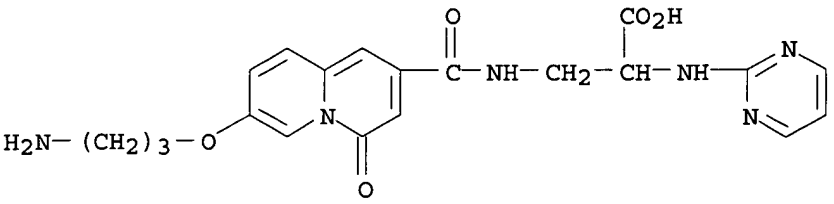
III

AB The quinolizinone (I) and tetrahydroquinolizinone analogs (II) (one of R1 and R2 = -J-K-L and other H ;(J = -(CH2)m-, -(CH2)mQ(CH2)n; K, L = (un)substituted alkyl,cycloalkyl, aryl, alkenyl etc); one of R3 and R4 = -X-Y-Z and other H (X,Y = -(CH2)m-, -(CH2)mQ(CH2)n; Z = H, CO2H, CO2R and SO2R, R = alkyl, cycloalkyl etc.) (Q = O, S, amino, CO2, etc.))where m, n, o and p are independently integer from 0-6, and their pharmaceutically acceptable salts, solvates or metabolic precursors were prepd. as effective inhibitors of **integrins**, particularly .alpha.IIb.beta.3 or .alpha.v **integrins** such as .alpha.v.beta.3 and .alpha.v.beta.5. Thus, compd. (III) (R5 = NHC(=NH)NH2, R6 = HCl) was prepd. by benzylation of 6-methyl-pyridin-3-ol followed by acetoxylation, oxidn., condensation with 2-(diethoxy-phosphoryl)-succinic acid di-Me ester, debenzylation, alkylation with 3-iodopropyl-carbamic acid tert-Bu ester, deesterification, condensation with (S)-3-amino-2-benzenesulfonylamino-propionic acid, treatment with trifluoroacetic acid and reacting trifluoroacetic acid salt of III (R5 = NH2, R6 = CF3CO2H) with 1H-pyrazole-1-carboxamidine hydrochloride. The IC50 of III for **integrins** .alpha.v.beta.3 and .alpha.IIb.beta.3 in fibrinogen binding assay was 0.015 and 0.0053.mu.M.

IT **262277-61-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(quinolizinones as **integrin** inhibitors)

RN 262277-61-2 CAPLUS

CN Alanine, 3-[[[7-(3-aminopropoxy)-4-oxo-4H-quinolizin-2-yl]carbonyl]amino]-N-2-pyrimidinyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 33 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:98336 CAPLUS
DOCUMENT NUMBER: 132:152134
TITLE: Preparation of heterocyclic-substituted amino acid derivatives as **integrin** receptor antagonists
INVENTOR(S): Duggan, Mark E.; Hartman, George D.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006169	A1	20000210	WO 1999-US16830	19990726
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2338275	AA	20000210	CA 1999-2338275	19990726
AU 9951286	A1	20000221	AU 1999-51286	19990726
AU 747784	B2	20020523		
EP 1100506	A1	20010523	EP 1999-935910	19990726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, LT, LV, FI, RO				
JP 2002521450	T2	20020716	JP 2000-562023	19990726
US 6040311	A	20000321	US 1999-362528	19990728

PRIORITY APPLN. INFO.: US 1998-94478P P 19980729
WO 1999-US16830 W 19990726
OTHER SOURCE(S): MARPAT 132:152134

AB Compds. W-X-Y-Z-CR5R6CR7R8CO2R9 [W is a 5- or 6-membered monocyclic arom. or nonarom. ring system or a 9- to 14-membered polycyclic ring system, where one or more of the rings is arom. and each ring system has 1, 2, 3, or 4 heteroatoms (N, O, S) and is optionally substituted; X = (un)substituted (CH2)v or (CH2)vNH(CH2)v (v = 0-6); Y = (un)substituted biaryl ring system comprising 5- or 6-membered arom. rings contg. 0-6 heteroaroms.; Z = CONH, NHCO, CH2CH2, or CH:CH which may be optionally substituted; R5-R9 = H or alkyl, aryl and other substituents] were prepd. as **integrin** receptor antagonists. Thus, 3'-[N-(3,4,5,6-tetrahydropyrimidin-2-yl)amino]biphenyl-4-carbonyl-2(S)-phenylsulfonylamino-.beta.-alanine was prepd. by a multistep scheme

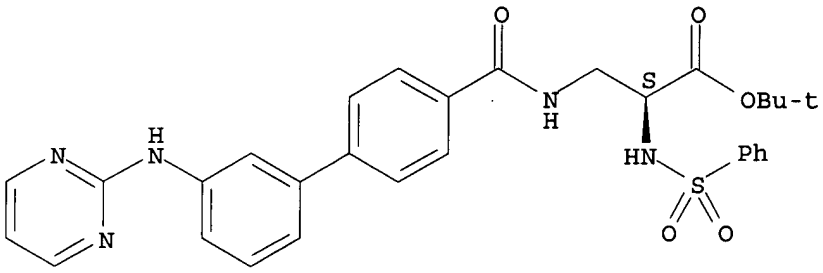
involving reactions of m-nitrobenzeneboronic acid, Me p-bromobenzoate, 2-bromopyrimidine, and 2(S)-phenylsulfonylamino-.beta.-alanine tert-Bu ester hydrochloride.

IT **257876-79-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of heterocyclic-substituted amino acid derivs. as **integrin** receptor antagonists)

RN 257876-79-2 CAPLUS

CN L-Alanine, N-(phenylsulfonyl)-3-[[[3'-(2-pyrimidinylamino)[1,1'-biphenyl]-4-yl]carbonyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 34 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:94016 CAPLUS

DOCUMENT NUMBER: 132:245846

TITLE: RGD mimetics containing a central hydantoin scaffold: .alpha.v.beta.3 vs .alpha.IIb.beta.3 selectivity requirements

AUTHOR(S): Peyman, Anusch; Wehner, Volkmar; Knolle, Jochen; Stilz, Hans Ulrich; Breipohl, Gerhard; Scheunemann, Karl-Heinz; Carniato, Denis; Ruxer, Jean-Marie; Gourvest, Jean-Francois; Gadek, Thomas R.; Bodary, Sarah

CORPORATE SOURCE: Hoechst Marion Roussel Deutschland GmbH, Frankfurt, D-65926, Germany

SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(2), 179-182
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

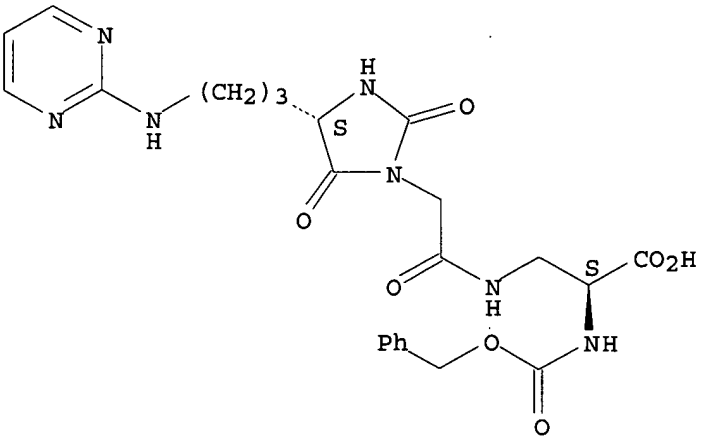
AB The synthesis of a series of RGD mimetic .alpha.v.beta.3 antagonists contg. a hydantoin scaffold is shown. The results demonstrate some of the structural requirements for the design of selective .alpha.v.beta.3 antagonists (vs. .alpha.IIb.beta.3) in terms of the Arg-mimetic, the distance between N- and C-terminus and the lipophilic side chain.

IT **197357-69-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(RGD mimetics contg. a central hydantoin scaffold in relation to .alpha.v.beta.3 vs. .alpha.IIb.beta.3 selectivity requirements)

RN 197357-69-0 CAPLUS

CN L-Alanine, 3-[[[(4S)-2,5-dioxo-4-[3-(2-pyrimidinylamino)propyl]-1-imidazolidinyl]acetyl]amino]-N-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



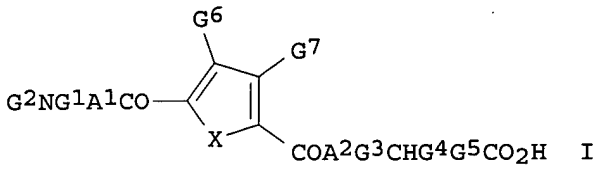
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:15198 CAPLUS
DOCUMENT NUMBER: 132:78464
TITLE: Preparation of thiophene-2,5-dicarboxamides and furan-2,5-dicarboxamides useful in the treatment of cancer
INVENTOR(S): Labrecque, Denis; Lamothe, Serge; Courchesne, Marc; Chan, Laval; Attardo, Giorgio; Meerovitch, Karen
PATENT ASSIGNEE(S): Biochem Pharma Inc., Can.
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000486	A1	20000106	WO 1999-IB1221	19990629
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9943853	A1	20000117	AU 1999-43853	19990629
EP 1091952	A1	20010418	EP 1999-926680	19990629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002137947	A1	20020926	US 2002-46396	20020116

PRIORITY APPLN. INFO.: US 1998-91063P P 19980629
WO 1999-IB1221 W 19990629
US 2000-736027 B1 20001221

OTHER SOURCE(S): MARPAT 132:78464
GI



AB The title compds. I [X = O, S; A1, A2 = O, S, N; G1, G3, G5 = alkyl chain; G2 = CHA3A4 with A3, A4 = O, N, S, etc.; G4 = aryl, arylsulfonylamino, arylamino; G6, G7 = H, F, Cl, iodo, Br, alkyl], useful in the treatment of cancer, were prepd. E.g., 3-{[5-(3-guanidinopropylcarbamoyl)thiophene-2-carbonyl]amino}-3-phenylpropionic acid was prepd. The IC50 values for fibrinogen binding assay of I were detd. Other properties of I, e.g. inhibition of metastasis in lung cancer model, were also detd.

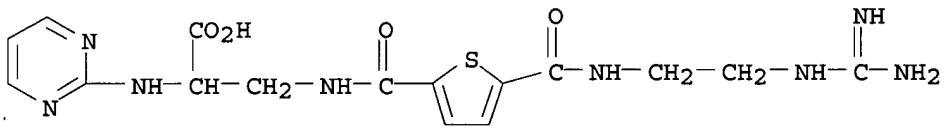
IT **253681-88-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of thiophenedicarboxamides and furandicarboxamides useful in the treatment of cancer)

RN 253681-88-8 CAPLUS

CN Alanine, 3-[[[5-[[[2-[(aminoiminomethyl)amino]ethyl]amino]carbonyl]-2-thienyl]carbonyl]amino]-N-2-pyrimidinyl-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

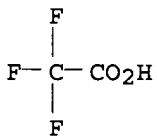
CM 1

CRN 253681-87-7
CMF C16 H20 N8 O4 S



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 36 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:672767 CAPLUS
DOCUMENT NUMBER: 131:299288
TITLE: Acylresorcinol derivatives as selective vitronectin receptor inhibitors

09/ 916,977

INVENTOR(S): Kees, Kenneth Lewis; Garrick, Lloyd Michael; Gopalsamy, Ariamala
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952879	A1	19991021	WO 1999-US8180	19990414
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9935610	A1	19991101	AU 1999-35610	19990414

PRIORITY APPLN. INFO.: US 1998-59579 19980414
WO 1999-US8180 19990414
OTHER SOURCE(S): MARPAT 131:299288
GI

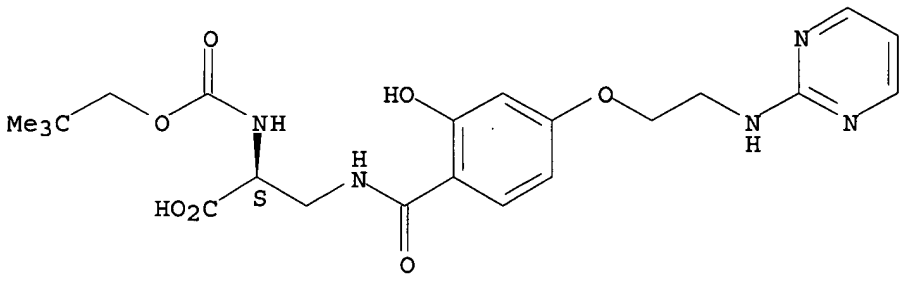
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. of formula I are useful in the treatment of various disorders including, but not limited to, cancer, angiogenesis, restenosis, inflammation, bone diseases, and as antiviral agents [wherein G = amidino and cyclic analogs, 2-pyridinyl, 2-pyrimidinyl, other similar N-contg. groups; R1, R2 = H, alkyl, aralkyl, heterocycloalkylalkyl; R3 = H, aryl, heterocycloalkyl; R4 = H, OH or NH2 or derivs.; provided that both R3 and R4 cannot be H; R5 = H, alkyl, optionally substituted with a terminal prodrug group; n = 1-4; and pharmaceutically acceptable salts]. Novel methods of making I are also provided. The compds. are selective inhibitors of certain **integrin** receptors such as .alpha.v.beta.3. Over 300 synthetic examples are given. For instance, the title compd. II.HCl was prepd. in 4 steps from the acid III, specifically: (1) amidation with 2S-(benzenesulfonylamino)-.beta.-alanine Et ester; (2) sapon. of the Et ester; (3) partial hydrogenation of the pyrimidine nucleus; and (4) acidic reesterification. II.HCl had an IC50 value of 0.12 .mu.M in an osteopontin-.alpha.v.beta.3 cell attachment assay, and 0.15 .mu.M in an osteoclast bone pitting assay.

IT **247124-79-4DP**, Wang resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of acylresorcinol derivs. as selective vitronectin receptor inhibitors)

RN 247124-79-4 CAPLUS
CN L-Alanine, N-[(2,2-dimethylpropoxy)carbonyl]-3-[[2-hydroxy-4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

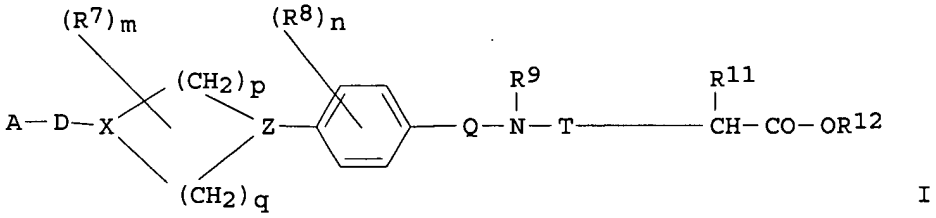


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 37 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:672755 CAPLUS
DOCUMENT NUMBER: 131:299455
TITLE: Preparation of aminopiperidine moiety-containing heterocyclic compounds as **integrin** .alpha.v.beta.3 antagonists
INVENTOR(S): Ishikawa, Minoru; Murakami, Shoichi; Yamamoto, Mikio; Kubota, Dai; Hachisu, Mitsugu; Katano, Kiyoaki; Ajito, Keiichi
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 192 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952872	A1	19991021	WO 1999-JP1903	19990409
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2327673	AA	19991021	CA 1999-2327673	19990409
AU 9931678	A1	19991101	AU 1999-31678	19990409
AU 759449	B2	20030417		
EP 1074543	A1	20010207	EP 1999-913611	19990409
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 507222	A	20030530	NZ 1999-507222	19990409
US 6420558	B1	20020716	US 2000-673017	20001010

PRIORITY APPLN. INFO.: JP 1998-97066 A 19980409
WO 1999-JP1903 W 19990409
OTHER SOURCE(S): MARPAT 131:299455
GI



I

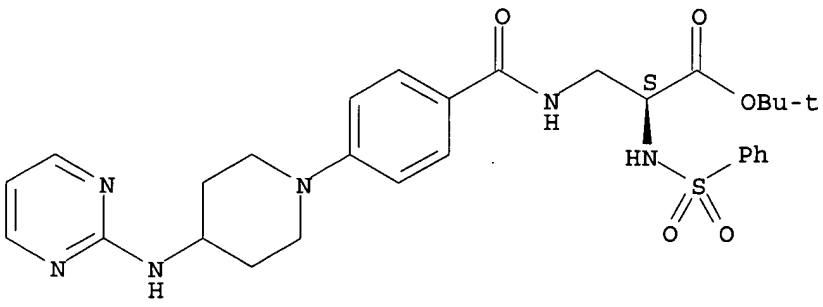
AB The title compds. I [A represents a 5- to 7-membered heterocycle contg. two nitrogen atoms; D represents NH2, CH2, etc.; X and Z represent each CH or N; R7 and R8 represent each alkyl, halogeno, etc.; Q represents CO, CH2, etc.; R9 represents H, alkyl, aralkyl, etc.; T = (CHR10)a; R10 represents H, alkynyl, etc.; R11 represents H, substituted amino, etc.; R12 represents H or alkyl; m is from 0 to 5; n is from 0 to 4; p and q are each from 1 to 3; and a is 0 or 1] are prepd. I have .alpha.v.beta.3 antagonism, cell adhesion inhibitory effect, GP IIb/IIIa antagonism and/or human platelet aggregation inhibitory effect. I are useful in the treatment of cardiovascular diseases, diseases in assocn. with neovascularization, cerebrovascular diseases, etc. In an in vitro test for **integrin** .alpha.v.beta.3 antagonism, 18 compds. of this invention showed IC50 values .ltoreq. 1 nM.

IT **247033-63-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminopiperidine moiety-contg. heterocyclic compds. as **integrin** .alpha.v.beta.3 antagonists)

RN 247033-63-2 CAPLUS

CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[4-(2-pyrimidinylamino)-1-piperidinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 38 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:640839 CAPLUS
DOCUMENT NUMBER: 131:271881
TITLE: Preparation of pyrimidinylalkylphenylcarbonylaminopropanoates and related compounds as **integrin** antagonists
INVENTOR(S): Pitts, William J.; Jadhav, Prabhakar K.
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Co., USA
SOURCE: PCT Int. Appl., 337 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9950249	A2	19991007	WO 1999-US6827	19990329
WO 9950249	A3	19991125		
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2333927	AA	19991007	CA 1999-2333927	19990329
AU 9932137	A1	19991018	AU 1999-32137	19990329
EP 1054871	A2	20001129	EP 1999-914248	19990329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2003504301	T2	20030204	JP 2000-541154	19990329
US 2001044535	A1	20011122	US 2001-828751	20010409
US 6489333	B2	20021203		

PRIORITY APPLN. INFO.: US 1998-80242P P 19980401
WO 1999-US6827 W 19990329
US 1999-282496 A3 19990331

OTHER SOURCE(S): MARPAT 131:271881

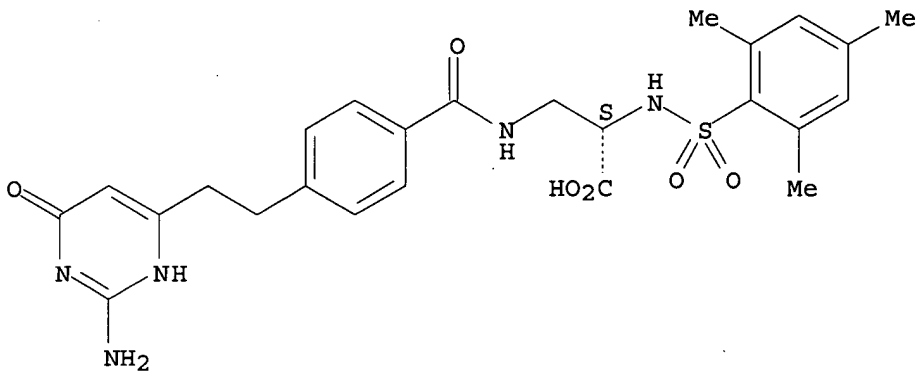
AB GT (T = **integrin** antagonist template; G = specified guanidine mimic), were prepd. as antagonists of the .alpha.v.beta.3 **integrin**, the .alpha.2b.beta.3 **integrin**, and related cell surface adhesive protein receptors for the inhibition of cell adhesion, treatment of angiogenic disorders, inflammation, bone degrdn., cancer metastasis, diabetic retinopathy, thrombosis, restenosis, macular degeneration, and other conditions mediated by cell adhesion and/or cell migration and/or angiogenesis. Thus, 2-[(S)-2,4,6-trimethylphenylsulfonylamino]-3-[4-[2-(2,4-diaminopyrimidin-6-yl)ethyl]phenylcarbonylamino]propionic acid trifluoroacetate was prepd. in several steps from L-asparagine. In the .alpha.v.beta.3-vitronectin assay, tested title compds. showed IC50.ltoreq.10 .mu.M.

IT **245527-29-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrimidinylalkylphenylcarbonylaminopropanoates and related compds. as **integrin** antagonists)

RN 245527-29-1 CAPLUS

CN L-Alanine, 3-[[4-[2-(2-amino-1,6-dihydro-6-oxo-4-pyrimidinyl)ethyl]benzoyl]amino]-N-[(2,4,6-trimethylphenyl)sulfonyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

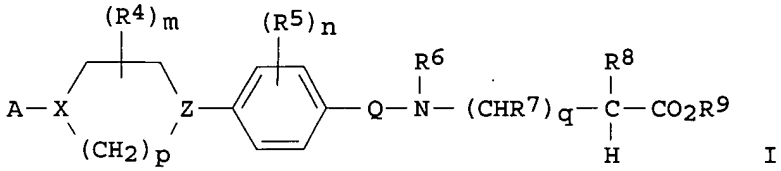


● Na

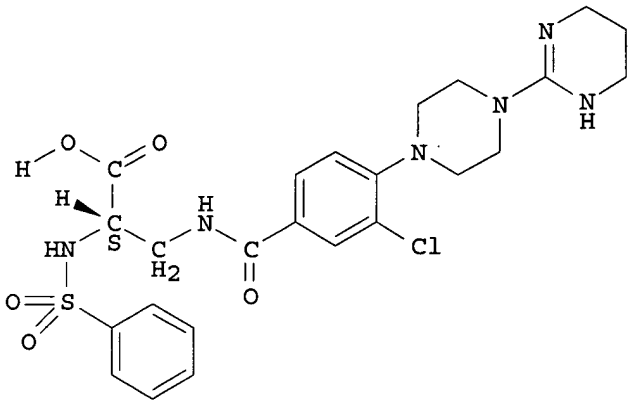
L4 ANSWER 39 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:495277 CAPLUS
DOCUMENT NUMBER: 131:130008
TITLE: Preparation of phenylpiperazine derivatives as **integrin** .alpha.v.beta.3 antagonists
INVENTOR(S): Ajito, Keiichi; Murakami, Shoichi; Ishikawa, Minoru; Yamamoto, Mikio; Kubota, Dai; Gomi, Shuichi; Hachisu, Mitsugu; Katano, Kiyoaki
PATENT ASSIGNEE(S): Meiji Seika Kaisha, Ltd., Japan
SOURCE: PCT Int. Appl., 162 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9938849	A1	19990805	WO 1999-JP415	19990201
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2319824	AA	19990805	CA 1999-2319824	19990201
AU 9920762	A1	19990816	AU 1999-20762	19990201
EP 1057818	A1	20001206	EP 1999-901205	19990201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6451800	B1	20020917	US 2000-601176	20000728

PRIORITY APPLN. INFO.: JP 1998-19282 A 19980130
WO 1999-JP415 W 19990201
OTHER SOURCE(S): MARPAT 131:130008
GI



I



II

AB Compds. represented by general formula (I) or pharmaceutically acceptable salts or solvates thereof [A = (un)satd. and (un)satd. 5- to 7-membered heterocycle contg. two nitrogen atoms, optionally fused to (un)satd. and (un)satd. 5- to 7-membered heterocycle, (un)substituted C(:NH)NH2; X, Z = CH, N; R4, R5 = (un)substituted C1-6 alkyl or alkoxy, halogeno, NH2, NO2, OH; Q CO, CH2, CHR10, CHOR10; wherein R10 = C1-6 alkyl; R6 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl or alkynyl, (un)substituted aralkyl; R7 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl or alkynyl, aralkyl, or NH2 ; R8 = H, (un)substituted C1-6 alkyl, C2-6 alkenyl, or C2-6 alkynyl, (un)substituted aralkyl or NH2; R9 = H, alkyl; m = 0 to 5; n = 0 to 4; p = 2 or 3; q = 0 or 1] are prepd. These compds. also exhibit potent antagonizing effect on blood platelet membrane protein GP IIb/IIa and potent inhibiting-effect on human blood platelet aggregation and are useful for the treatment of **integrin** .alpha.v.beta.3-mediated diseases such as cardiovascular diseases, neovascularization-related diseases, cancer or its metastasis, immune diseases, or bone diseases and useful as blood platelet aggregation inhibitors for the treatment of blood platelet thrombosis, thromboembolism, thrombocytopenic purpura, and hemolytic uremic syndrome, for improving peripheral blood circulation, and for inhibiting blood aggregation during exo-circulation. Thus, Me 2-chloro-4-(piperazin-1-yl)benzoate was condensed with 2-bromopyridine in the presence of (Me2CH)2NEt in DMF at 80.degree. for 5.0 h, followed by sapon. with a mixt. of 1 N NaOH, MeOH, and THF and acidification with 1 N HCl to give the title compd. (II). In a **integrin** .alpha.v.beta.3 binding assay, II in vitro showed IC50 of 3.5 nM .mu.g/mL for inhibiting the binding of vitronectin to vitronectin receptors.

IT **234080-72-9P**

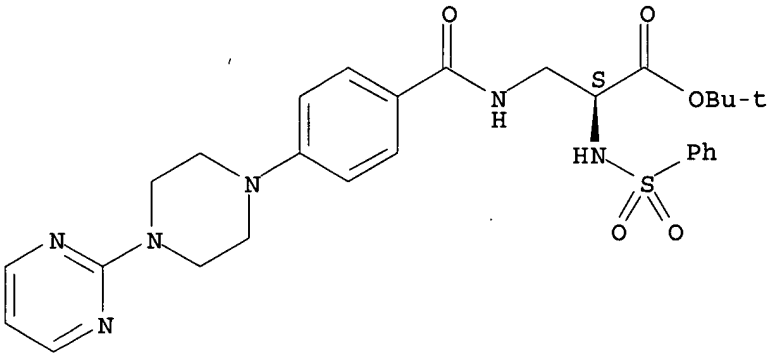
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of phenylpiperazine derivs. as **integrin** .alpha.v.beta.3 antagonists and blood platelet aggregation inhibitors for treatment of diseases)

RN 234080-72-9 CAPLUS

CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[4-(2-pyrimidinyl)-1-piperazinyl]benzoyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



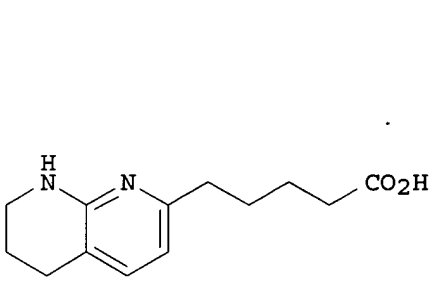
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 40 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:404930 CAPLUS
DOCUMENT NUMBER: 131:58766
TITLE: Heterocyclic-substituted carboxylic acid **integrin** receptor antagonists
INVENTOR(S): Askew, Ben C.; Coleman, Paul J.; Duggan, Mark E.; Halczenko, Wasyl; Hartman, George D.; Hunt, Cecilia; Hutchinson, John H.; Meissner, Robert S.; Patane, Michael A.; Smith, Garry R.; Wang, Jiabing
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 249 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

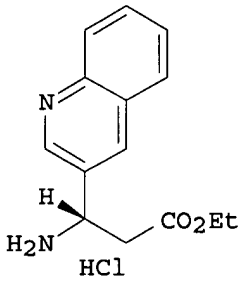
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931061	A1	19990624	WO 1998-US26484	19981214
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2315220	AA	19990624	CA 1998-2315220	19981214
AU 9918220	A1	19990705	AU 1999-18220	19981214
AU 739811	B2	20011018		
EP 1040098	A1	20001004	EP 1998-963136	19981214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9813769	A	20001010	BR 1998-13769	19981214
EE 200000362	A	20011217	EE 2000-200000362	19981214
JP 2002508355	T2	20020319	JP 2000-538988	19981214
NZ 504893	A	20021025	NZ 1998-504893	19981214
US 6048861	A	20000411	US 1998-212082	19981215
US 6297249	B1	20011002	US 1999-453847	19991202
NO 2000003114	A	20000816	NO 2000-3114	20000616
HR 2000000401	A1	20011231	HR 2000-401	20000616
BG 104605	A	20010531	BG 2000-104605	20000713

09/ 916,977

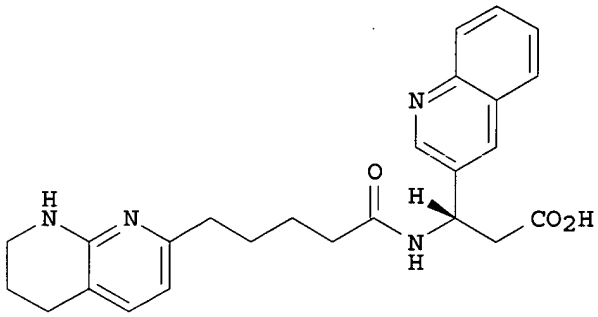
US 2002010176 A1 20020124 US 2001-916977 20010728
PRIORITY APPLN. INFO.: US 1997-69899P P 19971217
GB 1998-7382 A 19980406
US 1998-83209P P 19980427
GB 1998-11295 A 19980526
US 1998-92622P P 19980713
US 1998-108063P P 19981112
WO 1998-US26484 W 19981214
US 1998-212082 A3 19981215
US 1999-454847 A3 19991207
OTHER SOURCE(S): MARPAT 131:58766
GI



I



II



III

AB The substituted carboxylic acids R-X-X1-CR5R6-CR7R8-CO2R9 [R = R1R2NC(:NR1), R1R2NC(:NR1)NR1, 5- or 6-membered nitrogen, oxygen, and/or sulfur heterocyclyl with nitrogen substituted by R1; X = (CH2)m, (CH2)mO(CH2)n, (CH2)mNR4(CH2)n, (CH2)mS(CH2)n, (CH2)mSO(CH2)n, (CH2)mO(CH2)nO(CH2)p, (CH2)mO(CH2)nNR4(CH2)p, etc.; X1 = -CONR4-, -NR4CO-, -NR4CONR4-, and -CH2CH2- or -CH:CH- substituted by R3; R1, R2 = H, halo, alkyl, cycloalkyl, amino, acylamino, alkoxycarbonyl, F3CO, alkylsulfonylamino, etc.; R3 = H, aryl, alkyl, arylalkoxyalkyl, arylalkylaminoalkyl, halo, F3C, H2N, arylaminocarbonyl, etc.; R4 = H, aryl, H2NCO, alkyl, arylalkyl, aryloxycarbonyl, H2SO2, arylsulfonyl, etc.; R5, R6, R7, R8 = H, alkyl, aryl, arylalkoxyalkyl, arylalkylaminoalkyl, halo, HO, H2N, H2NCO, etc.; R9 = H, alkyl, aryl, alkylaminocarbonylmethylene, etc.] and their pharmaceutically acceptable salts were prepd for use as **integrin** receptor antagonists (no data). Thus, amidation of the tetrahydronaphthyridinylpentanoate I with the aminoquinolinepropionate II and subsequent sapon. gave the (quinolinyl)naphthyridinylpentanoylaminopropionate III. More particularly, the compds. of the present invention are antagonists of the **integrin** receptors .alpha..nu..beta.3, .alpha..nu..beta.5, and/or .alpha..nu..beta.6 and are useful for inhibiting bone resorption, treating and preventing osteoporosis, and inhibiting vascular restenosis, diabetic

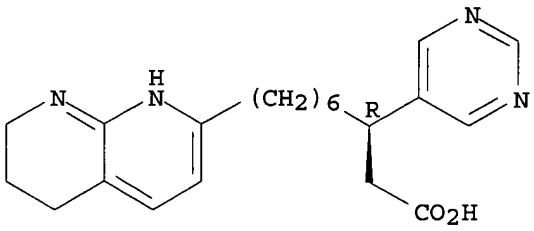
retinopathy, clear degeneration, angiogenesis, atherosclerosis, inflammation, wound healing, viral disease, tumor growth, and metastasis.

IT **227752-23-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclic-substituted carboxylic acids as **integrin** receptor antagonists)

RN 227752-23-0 CAPLUS

CN 1,8-Naphthyridine-2-nonanoic acid, 1,5,6,7-tetrahydro-.beta.-5-pyrimidinyl-, (.beta.R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 41 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:677821 CAPLUS
DOCUMENT NUMBER: 129:302890
TITLE: Treatment of cancer using a combination of **integrin** antagonists and farnesyl protein transferase inhibitors.
INVENTOR(S): Duggan, Mark E.; Hartman, George D.; Heimbrook, David C.; Oliff, Allen I.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 422 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9844797	A1	19981015	WO 1998-US6823	19980406
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9869532	A1	19981030	AU 1998-69532	19980406
AU 724216	B2	20000914		
EP 973396	A1	20000126	EP 1998-915318	19980406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001524079	T2	20011127	JP 1998-543013	19980406

PRIORITY APPLN. INFO.: US 1997-41923P P 19970407
GB 1998-976 A 19980116
WO 1998-US6823 W 19980406

OTHER SOURCE(S): MARPAT 129:302890

09/ 916,977

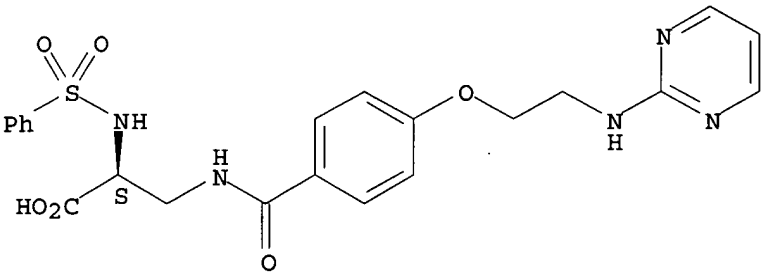
AB A method of achieving a therapeutic effect comprising administration of an **integrin** antagonist and a farnesyl-protein transferase inhibitor where the amt. of either alone is insufficient to achieve the effect, is claimed (no data). Amino acid and peptide derivs., e.g., N-[(2R)-amino-3-mercaptopropyl]valylisoleucylleucine, were prepd.

IT **174665-30-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of cancer using a combination of **integrin** antagonists and farnesyl protein transferase inhibitors)

RN 174665-30-6 CAPLUS

CN L-Alanine, N-(phenylsulfonyl)-3-[[4-[2-(2-pyrimidinylamino)ethoxy]benzoyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



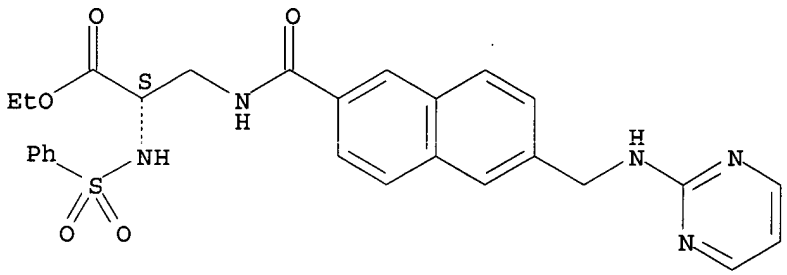
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 42 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:293369 CAPLUS
DOCUMENT NUMBER: 128:321934
TITLE: Preparation of amino acid derivatives as **integrin** antagonists
INVENTOR(S): Duggan, Mark E.; Hartman, George D.; Hoffman, William F.; Ihle, Nathan C.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Duggan, Mark E.; Hartman, George D.; Hoffman, William F.; Ihle, Nathan C.
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818461	A1	19980507	WO 1997-US19349	19971027
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9850884	A1	19980522	AU 1998-50884	19971027
AU 717283	B2	20000323		
EP 946164	A1	19991006	EP 1997-913775	19971027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001504456	T2	20010403	JP 1998-520639	19971027

US 5919792 A 19990706 US 1997-959662 19971028
PRIORITY APPLN. INFO.: US 1996-29223P P 19961030
GB 1996-26308 A 19961218
WO 1997-US19349 W 19971027
OTHER SOURCE(S): MARPAT 128:321934
AB Amino acids derivs. X-Y-Z-Ring-A-B [Ring is a mono- or polycyclic ring system; X = NR1R2, NR1CR3:NR2, C(:NR2)NHR4, NR1C(:NR2)NR3R4, aryl-NR1R2, aryl-C(:NR1)NR2R3, aryl-NR1C(:NR2)NR3R4, (R1-R4 = H, halo, alkyl, arylalkyl, aminoalkyl, etc.), a mono- or polycyclic ring system; Y = alkylene, imino-, carbonyl-, oxydialkylene, etc.; Z = (CH2)m, (CH2)mO(CH2)n, (CH2)mC.tplbond.C(CH2)n, etc. (m, n = 0-6); A = (CH2)qO(CH2)p, (CH2)qCS(CH2)p (p, q = 0-6), etc.; B = (un)substituted carboxy- or carbamoylalkyl, including amino acid residues] were prepd. as vitronectin receptor antagonists. Thus, 4-[2-(2-aminopyridin-6-yl)ethyl]benzoyl-2(S)-[[(4-125iodophenyl)sulfonyl]amino]-.beta.-alanine was prepd. and used in a formulation for inhibition of bone resorption.
IT **206997-23-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of amino acid derivs. as **integrin** antagonists)
RN 206997-23-1 CAPLUS
CN L-Alanine, N-(phenylsulfonyl)-3-[[[6-[(2-pyrimidinylamino)methyl]-2-naphthalenyl]carbonyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 43 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:684277 CAPLUS
DOCUMENT NUMBER: 127:331749
TITLE: Preparation of peptidyl isoindolone derivatives as .alpha.v.beta.3 receptor antagonists
INVENTOR(S): Duggan, Mark E.; Hartman, George D.; Hoffman, William F.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Duggan, Mark E.; Hartman, George D.; Hoffman, William F.
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9737655	A1	19971016	WO 1997-US5890	19970408

W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU,

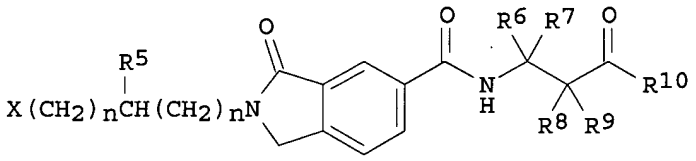
IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX,
NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN,
YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,
ML, MR, NE, SN, TD, TG

CA 2251017	AA	19971016	CA 1997-2251017	19970408	
AU 9724501	A1	19971029	AU 1997-24501	19970408	
AU 720758	B2	20000608			
EP 901373	A1	19990317	EP 1997-920270	19970408	
EP 901373	B1	20021106			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
US 5925655	A	19990720	US 1997-841979	19970408	
JP 2000508319	T2	20000704	JP 1997-536469	19970408	
AT 227268	E	20021115	AT 1997-920270	19970408	
ES 2185009	T3	20030416	ES 1997-920270	19970408	

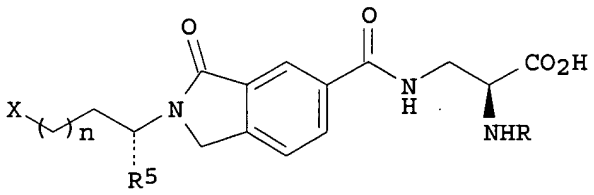
PRIORITY APPLN. INFO.: US 1996-15177P P 19960410
GB 1996-10996 A 19960524
WO 1997-US5890 W 19970408

OTHER SOURCE(S): MARPAT 127:331749

GI



I



II

AB The prepn. of novel peptidyl isoindolone compds. I [X = NR1C(:NR3R4):NR2, Ar, NR1Ar; Ar = optionally substituted, 4-10 membered mono- or polycyclic arom. or nonarom. ring contg. 0-4 N, O, or S atoms; R1-R4 = independently H, OH, C1-8 alkyl, halo, aryl-C0-8 alkyl, (un)substituted C1-6 alkylamino, C1-4 alkoxy-C0-8 alkyl, carboxy-C0-8 alkyl, C3-8 cycloalkyl-C0-6 alkyl, etc; R5 = H, C1-6 alkyl, C0-6 alkylaryl, aryl, C3-8 cycloalkyl-C0-6 alkyl; R6-R9 = independently F, any group R1-R4, C1-6 alkoxy, (un)substituted C1-6 alkylcarbonyl, etc; R10 = OH, C1-8 alkoxy, aryl-C0-6 alkoxy, C1-8 alkylcarbonyloxy-C1-4 alkoxy, aryl-C1-8 alkylcarbonyloxy-C1-4 alkoxy, C1-6 dialkylaminocarbonylmethoxy, aryl-C1-6 dialkylaminocarbonylmethoxy, D- or L-amino acid or amino acid ester; n = independently 0-3; with provisos] and derivs. thereof, and their use as .alpha.v.beta.3 receptor antagonists is described. These .alpha.v.beta.3 receptor antagonists are useful for inhibiting bone resorption, treating and preventing osteoporosis and cancer, and inhibiting vascular restenosis, diabetic retinopathy, macular degeneration, angiogenesis, atherosclerosis, inflammation and tumor growth. Thus, isoindolone derivs. II [X = C(NH2):NH, 2-pyridyl, 1,4,5,6-tetrahydropyrimidin-2-yl; R5 = H, Me; n = 0, 1; R = SO2Ph, CO2CH2Ph, 2-pyridylsulfonyl] were prepd. via cyclocondensation of di-Me 4-bromomethyl-1,3-benzenedicarboxylate with ethylenediamine or

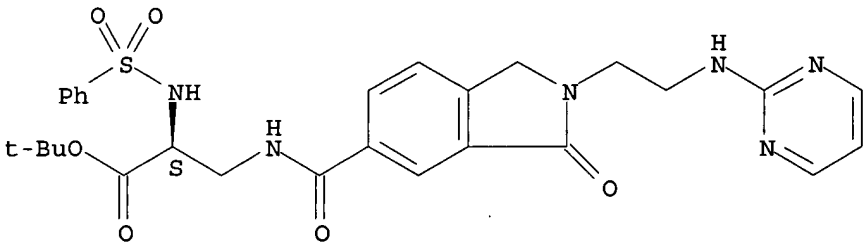
propanediamine derivs., coupling with 2,4-diaminopropanoic acid derivs, guanylation or arylation, and deprotection. Prepd. compds. II bind to human .alpha.v.beta.3 **integrin** with IC50 = 0.47-415 nM in an EIB assay.

IT **197964-71-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptidyl isoindolone derivs. as .alpha.v.beta.3 receptor antagonists)

RN 197964-71-9 CAPLUS

CN L-Alanine, 3-[[[2,3-dihydro-3-oxo-2-[2-(2-pyrimidinylamino)ethyl]-1H-isoindol-5-yl]carbonyl]amino]-N-(phenylsulfonyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 44 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:674730 CAPLUS
DOCUMENT NUMBER: 127:341553
TITLE: The in vitro and in vivo pharmacological profiles of a platelet glycoprotein IIb/IIIa antagonist, NSL-9403
AUTHOR(S): Katada, Jun; Takiguchi, Yoshimi; Muramatsu, Michiko; Fujiyoshi, Toshio; Uno, Isao
CORPORATE SOURCE: Advanced Technology Research Laboratories, Life Science Research Center, Nippon Steel Corporation, Kawasaki, 211, Japan
SOURCE: Thrombosis Research (1997), 88(1), 27-40
CODEN: THBRAA; ISSN: 0049-3848
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The in vitro and in vivo pharmacol. profiles of NSL-9403 [orotyl-seryl-arginyl-glycyl-aspartyl-tryptophane], a platelet glycoprotein IIb/IIIa (GpIIb/IIIa) antagonist, has been studied. NSL-9403 inhibited platelet aggregation of human platelet-rich plasma (PRP) with IC50 values of 4.3 .mu.M (collagen) and 1.8 .mu.M (ADP), which was about 100 times more potent than RGDS. It also inhibited the binding of fibrinogen to activated platelets. Ex vivo collagen and ADP-induced platelet aggregation in a guinea pig was inhibited after a bolus i.v. administration of NSL-9403 at 1.25 mg/kg and above. NSL-9403 had an antithrombotic effect in in vivo thrombosis models. In a platelet agonist-induced pulmonary embolic sudden death model, where a bolus injection of collagen and epinephrine induced sudden death in mice, i.v. administration of NSL-9403 before an injection of collagen and epinephrine inhibited this platelet-agonist induced death in a dose dependent manner. In an arterio-venous shunt, infusion of NSL-9403 at 3 mg/kg/h prevented an increase in circulation pressure due to thrombus formation in the shunt circuit and platelet loss. Infusion of NSL-9403 at 1 to 10 mg/kg/h produced a complete inhibition of platelet-dependent arterial thrombosis in a dog femoral arterial thrombosis model. Thus NSL-9403 is a potent inhibitor or platelet aggregation in vitro and a potent anti-thrombotic

agent in vivo with a relatively short duration of action.

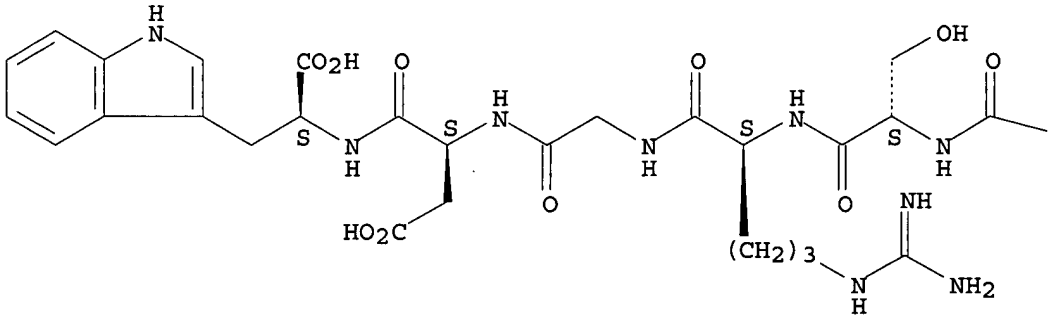
IT **158183-57-4**, NSL-9403
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro and in vivo pharmacol. profiles of a platelet glycoprotein IIb/IIIa antagonist NSL-9403)

RN 158183-57-4 CAPLUS

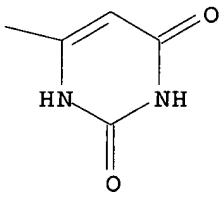
CN L-Tryptophan, 1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinecarbonyl-L-seryl-L-arginylglycyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L4 ANSWER 45 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1997:290093 CAPLUS

DOCUMENT NUMBER: 126:264011

TITLE: Preparation of meta-guanidine, urea, thiourea or azacyclic amino benzoic acid derivatives as **integrin** antagonists

INVENTOR(S): Ruminski, Peter Gerrard; Clare, Michael; Collins, Paul Waddell; Desai, Bipinchandra Nanubhai; Lindmark, Richard John; Rico, Joseph Gerace; Rogers, Thomas Edward; Russell, Mark Andrew; et al.

PATENT ASSIGNEE(S): G.D. Searle & Co., USA; Ruminski, Peter Gerrard; Clare, Michael; Collins, Paul Waddell; Desai, Bipinchandra Nanubhai; Lindmark, Richard, John

SOURCE: PCT Int. Appl., 930 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

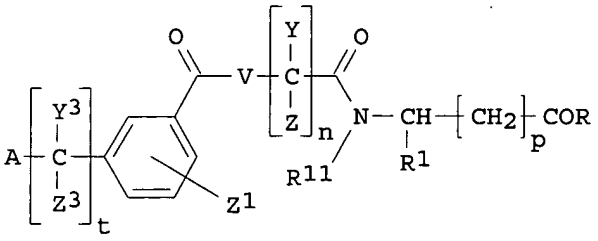
09/ 916,977

FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

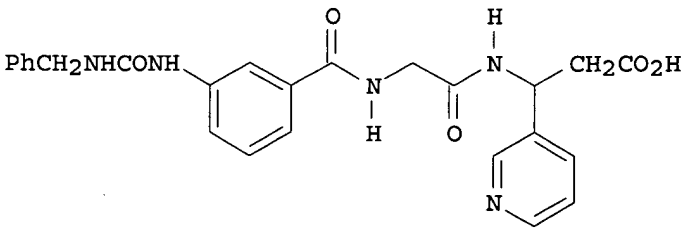
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9708145	A1	19970306	WO 1996-US13500	19960827
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
CA 2230209	AA	19970306	CA 1996-2230209	19960827
AU 9671039	A1	19970319	AU 1996-71039	19960827
AU 702487	B2	19990225		
EP 850221	A1	19980701	EP 1996-932142	19960827
EP 850221	B1	20010718		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1201454	A	19981209	CN 1996-197911	19960827
CN 1085980	B	20020605		
BR 9610422	A	19990713	BR 1996-10422	19960827
JP 11510814	T2	19990921	JP 1996-510397	19960827
IL 123164	A1	20010319	IL 1996-123164	19960827
AT 203234	E	20010815	AT 1996-932142	19960827
ES 2161373	T3	20011201	ES 1996-932142	19960827
RU 2196769	C2	20030120	RU 1998-105408	19960827
RO 118290	B1	20030430	RO 2001-1069	19960827
RO 118289	B1	20030430	RO 1998-500	19960827
ZA 9607379	A	19980330	ZA 1996-7379	19960830
NO 9800817	A	19980424	NO 1998-817	19980226
HK 1021532	A1	20020208	HK 1998-114666	19981228

PRIORITY APPLN. INFO.: US 1995-3277P P 19950830
WO 1996-US13500 W 19960827

OTHER SOURCE(S): MARPAT 126:264011
GI



I



II

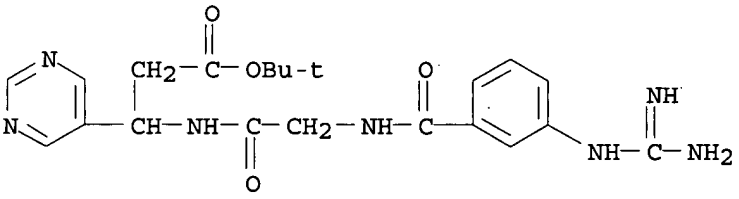
AB The title compds. I [A = (un)substituted ureido, guanidino, etc. (generic structures given); Z1 = H, alkyl, OH, alkoxy, halo, (di)(alkyl)amino, aryl, etc.; V = NR6; R6 = H, alkyl, etc.; or YR6 forms a 4- to 12-membered mono-N-contg. ring; Y, Y3, Z, Z3 = H, alkyl, aryl, cycloalkyl; or YZ or

Y3Z3 form cycloalkyl; n = 1-3; t = 0-2; p = 0-3; R = XR3; X = O, S, NH, etc.; R3 = H, alkyl, etc.; R1 = H, alkyl, alkenyl, etc.; R11 = H, alkyl, aralkyl, etc.] are prepd. For example, m-nitrohippuric acid was subjected to a sequence of (1) amidation with Et 3-amino-3-(3-pyridyl)propanoate-2HCl; (2) hydrogenation of the nitro group; (3) reaction of the formed amine with benzyl isocyanate; and (4) alk. sapon. of the ester, to give title compd. II, isolated as the CF3CO2H or HCl salt. In an in vitro assay for antagonism of human vitronectin receptor (.alpha.V.beta.3), the title compd. II.HCl bound with an IC50 of 0.86 nM.

IT **188810-02-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of meta-guanidino, -ureido, -thioureido, or -azacyclic-amino benzoic acid derivs. as **integrin** antagonists)

RN 188810-02-8 CAPLUS

CN .beta.-Alanine, N-[3-[(aminoiminomethyl)amino]benzoyl]glycyl-3-(5-pyrimidinyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1996:398904 CAPLUS

DOCUMENT NUMBER: 125:131630

TITLE: Design and synthesis of new antagonist peptides for platelet GPIIb/IIIa receptor as anti-thrombotic agents

AUTHOR(S): Hayashi, Uoshio; Sato, Yoshimi; Katada, Jun; Takiguchi, Yoshimi; Ojima, Iwao; Uno, Isao

CORPORATE SOURCE: Life Sci. Res. Center, Nippon Steel Corporation, Kawasaki, 211, Japan

SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(12), 1351-1356
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The structure-activity relationships of N-terminal modified RGD peptides against platelet aggregation inhibitory activity were studied, and Orotyl-Ser-Arg-Gly-Asp-Trp (NSL-9403) was a new and effective anti-thrombotic agent during extracorporeal circulation.

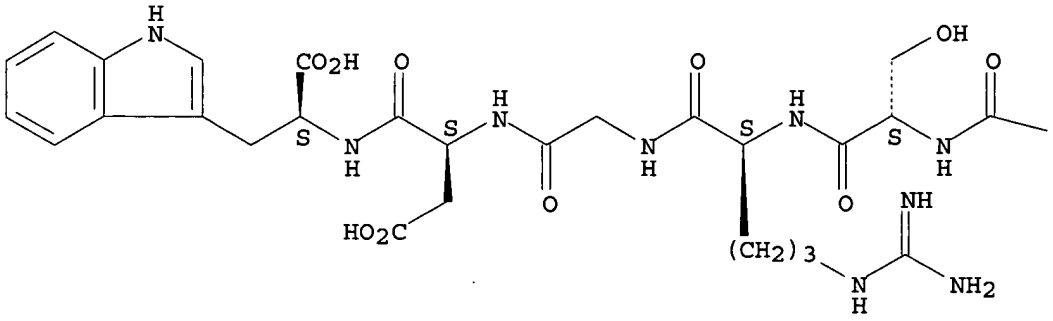
IT **158183-57-4P**, NSL-9403
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(design and synthesis of new antagonist peptides for platelet GPIIb/IIIa receptor as anti-thrombotic agents in relation to structure)

RN 158183-57-4 CAPLUS

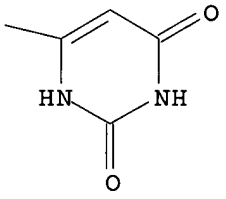
CN L-Tryptophan, 1,2,3,6-tetrahydro-2,6-dioxo-4-pyrimidinecarbonyl-L-seryl-L-arginylglycyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

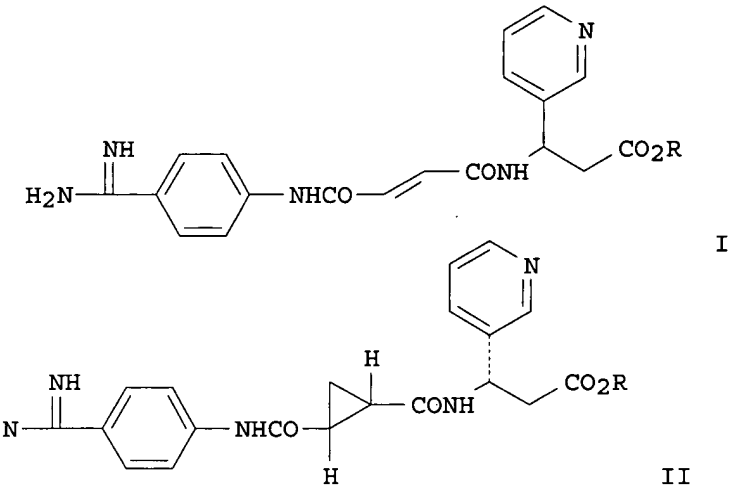


PAGE 1-B



L4 ANSWER 47 OF 47 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:328908 CAPLUS
DOCUMENT NUMBER: 122:240416
TITLE: Design of orally active, non-peptide fibrinogen receptor antagonists. An evolutionary process from the RGD sequence to novel antiplatelet aggregation agents
AUTHOR(S): Bovy, P. R.; Tjoeng, F. S.; Rico, J. G.; Rogers, T. E.; Lindmark, R. J.; Zablocki, J. A.; Garland, R. B.; McMackins, D. E.; Dayringer, H.; et al.
CORPORATE SOURCE: Thrombosis Research, Searle, Skokie, IL, 60077, USA
SOURCE: Bioorganic & Medicinal Chemistry (1994), 2(9), 881-95
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

II

AB The evolutionary process from the Arg-Gly-Asp-Phe (RGDF) tetrapeptide to potent orally active antiplatelet agents is presented. The RGD sequence is an important component in the recognition of fibrinogen by its platelet receptor GP IIb-IIIa (**integrin** .alpha.IIb.beta.3). This work concs. on the replacement of the Arg-Gly dipeptidyl fragment by an acylated aminobenzamidine. The C-terminal fragment has been replaced by a variety of .beta.-amino acids, expanding on a previously reported paradigm. The lead compds. showed good potency in an in vitro platelet aggregation assay (dog PRP/ADP). The affinity for the fibrinogen receptor was confirmed in several cases by the ability to inhibit 235I fibrinogen binding to activated human platelets. The Et ester prodrug form was tested by oral administration to dogs and monitoring of the anti-platelet effect on ex vivo collagen induced platelet aggregation. From the structural studies reported, the (amidinophenyl)succinamic acid deriv. 4-[HN:C(NH2)]C6H4NHCOCH2CH2CO2H was the best surrogate for the Arg-Gly dipeptide. Several conformationally restricted analogs are also reported which are compatible with the hypothesis of RGD binding to the .alpha.IIb.beta.3 in a turn-extended-turn conformation. The structure-activity relationships described also underline the importance of the .beta.-amino acid substitution for potency. In particular, the abs. configuration at the .beta.-carbon was crucial for high affinity. The best acid/ester pairs (I and II; R = H, Et) reported in this study had high potency (R = H; PRP/ADP IC50 .simeq. 50 nM) and showed good oral activity in dogs at 5 mg/kg per os (R = Et).

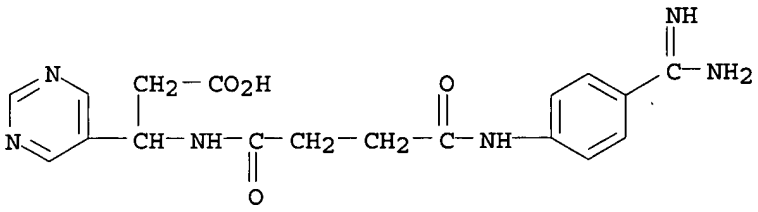
IT **149519-85-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(design and synthesis of orally active nonpeptide fibrinogen receptor antagonists)

RN 149519-85-7 CAPLUS

CN 5-Pyrimidinepropanoic acid, .beta.-[[4-[[4-(aminoiminomethyl)phenyl]amino]-1,4-dioxobutyl]amino]- (9CI) (CA INDEX NAME)



=> d his

(FILE 'HOME' ENTERED AT 09:19:07 ON 01 OCT 2003)

FILE 'REGISTRY' ENTERED AT 09:19:20 ON 01 OCT 2003
L1 STRUCTURE UPLOADED
L2 3960 S L1 FUL

FILE 'CAPLUS' ENTERED AT 09:21:39 ON 01 OCT 2003
L3 1280 S L2
L4 47 S L3 AND INTEGRIN?

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	219.92	369.48
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-30.60	-30.60

STN INTERNATIONAL LOGOFF AT 09:28:35 ON 01 OCT 2003